

1968

# The design of an artificial ventricle and its power and control systems

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SWIFT, Curran Stewart, 1940-  
THE DESIGN OF AN ARTIFICIAL VENTRICLE  
AND ITS POWER AND CONTROL SYSTEMS.

Iowa State University, Ph.D., 1968  
Engineering, biomedical

University Microfilms, Inc., Ann Arbor, Michigan

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1968

THE DESIGN OF AN ARTIFICIAL VENTRICLE  
AND ITS POWER AND CONTROL SYSTEMS

by

Curran Stewart Swift

A Dissertation Submitted to the  
Graduate Faculty in Partial Fulfillment of  
The Requirements for the Degree of  
Doctor of Philosophy

Major Subject: Electrical Engineering

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1968

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## INTRODUCTION

The chief purpose of this dissertation is to document the design and performance of an automatically-regulated artificial ventricle used for short-term animal experiments. The overall objective of the work was to develop an artificial ventricle system of low biological reactance (physically, chemically, and functionally) for studies of regulation of the pulmonary and systemic blood vascular systems in experimental animals. A major aim was a study of various combinations of animal-machine feedback control mechanisms in order to find the most appropriate physiologic parameter or combination of parameters which must be monitored and utilized to regulate the fluid output of the artificial ventricles in response to a subject's changing circulatory requirements. This objective was, in part, accomplished by use of the capabilities of an artificial ventricle system herein described.

To adequately provide, by electromechanical means, the exact functional duplication of and substitution for any living organ can be a prodigious task. However, once the principal overall function of the organ is defined and understood, the design of a device (or, more likely, a system) to reproduce just that function can be undertaken.

The heart is an organ which lends itself very well to an easy understanding and exact definition of its principal

function, that of being basically a pump. Its primary purpose is to provide a pulsatile blood flow to all the cells in the body for tissue oxygenation, nourishment, and removal of wastes.

This apparently simple job asked of the heart is not at first what it seems to be. The heart is a strong muscular organ about the size of a large fist and weighs approximately  $1/300$  of the body weight (123). To keep all the blood in the body (about eight percent of the body weight) in continual circulation through the miles of blood vessels, the normal heart is called upon to perform the following minimal tasks.

1. It must contract about 72 times each minute or more than 100,000 times each day.
2. It must pump about five liters of blood each minute or about 7200 liters (1900 gallons) each day.
3. Its power requirement is about 3.73 watts (51). This is an energy requirement of 88.5 watt-hours per day. If this energy were available directly from an electric utility company, the cost per year, at four cents per kilowatt-hour, would be \$1.30!

The normal heart has a resting duty cycle of about 67 percent. But it can double both its rate and fluid output during periods of strenuous physical exercise or emotional

strain. The faster the heart beats the harder it works and the less time it has to rest.

Considering the work the heart is called upon to deliver, it is not surprising that nearly a fourth of the U.S. adult population lives under a threat of heart disease and that there are more than 500,000 deaths each year from coronary artery disease (63). This means that heart disease is the top killer in the U.S. today, and strokes rank third, just behind cancer. But heart disease and strokes both develop from arterial diseases and together they account for 75 percent of all U.S. deaths (116). The conclusion to be drawn, then, is that cardiovascular disease is probably the most pressing problem of modern medicine.

Considerable money and research effort has been expended in combating this many-sided heart disease problem. The fight has been greatly aided by many new drugs, surgical and recovery procedures, ideas, materials, and machines. The use of heart-lung machines outside the body for temporary maintenance of circulation during heart surgery is well known.

However, there are many patients with irreversibly damaged hearts who cannot benefit from cardiac surgery at the present stage of technical development. Total replacement of the heart is perhaps the only way the lives of these persons could be saved. The possibility of being able to transplant a living heart into the human body may offer



a solution. But this creates a dilemma -- not only are there immunologic problems but also there exists the difficulty of procuring either a human or an animal heart. According to Nosé (89) there are approximately only 500 potential donors of the heterologous heart if the chimpanzee must be relied upon.

Probably as an extension of the heart-lung machine came the idea of the replacement of a patient's failing heart with a mechanical one to take over completely and permanently the function of the natural heart. Recent engineering progress has made the permanent replacement of the human heart with an intrathoracic artificial heart a definite possibility for the future.

Regardless of how the time sequence of thoughts for heart replacement went, the first experimenter to attempt the implantation of a mechanical heart inside the body was apparently V.P. Demikhov, a Soviet investigator (63). In 1937 he performed three experiments in which a pumping device was implanted in animals. The pump was externally driven by a rotating shaft inserted into the animal through a tube in the chest wall. Probably the first artificial heart experiment in the U.S. was performed in December, 1957, at the Cleveland Clinic. An air-driven artificial heart was implanted inside the chest of a dog, and the animal survived for 90 minutes (63). There are now in excess of 30 groups engaging in research on and development

of artificial hearts and closely allied problems. The group with which the author has been associated is one of the 30. The Iowa State University Artificial Heart Program has devoted its effort to the development of both heart models and control systems. The research was supported by Iowa State University, the Iowa Heart Association, the American Heart Association, and the Iowa State University Affiliate Program in Solid State Electronics.

To gain a better understanding of the problems involved in developing an artificial ventricle and its power and control systems, the anatomy and physiology of the normal intact heart will be described. The description will also include a discussion of the normal heart's accompanying loads (pulmonary and systemic circulatory systems) and control mechanisms (nervous, humoral, and intrinsic). Following this, various important aspects of mechanical artificial hearts in general (ideal specifications, types of pumps already developed, materials and valves, blood trauma, power, and control) will be discussed. This section will conclude with a description of various cardiac devices which are designed for short-term assistance of a malfunctioning but recuperating natural heart. Then the artificial ventricles developed in this study and their power and control systems will be documented and the experimental results, both in vivo and in vitro, will be discussed.

## THE CARDIOVASCULAR SYSTEM

### General Outline of the Cardiovascular System

Figure 1 shows the general plan of the human circulatory system. In the figure, all the arteries and veins are shown as single large distensible chambers. The actual system consists of a network of blood vessels and the heart which pumps blood through them. The heart is composed of four chambers: right and left atria and right and left ventricles. The atria, although acting as weak pumps to transfer blood from the systemic and pulmonary veins to the ventricles, primarily serve as entryways for the two ventricles. The ventricles provide the main propelling force to move the blood.

There are two major subdivisions of the circulatory system, the systemic circulation and the pulmonary circulation. From the right ventricle blood enters the pulmonary artery, passes through the lungs, and returns via the pulmonary veins to the left atrium, thus completing the pulmonary circulation. From the left atrium blood flows into the left ventricle, then through the aorta and its branches to all parts of the body, and, returning to the heart, enters the right atrium, thus completing the systemic circulation.

The aorta and the pulmonary artery undergo repeated

division with successive branches (arteries) gradually diminishing in size. The smallest arterial branches are called arterioles. The arterioles divide to form the network of capillaries which are the smallest of all the blood vessels. Then the post-capillary vessels undergo a progressive increase in size. Capillaries join to form small veins or venules, which in turn combine to give rise to the larger veins. These become bigger as they receive additional tributaries, until they finally form the large veins which enter the heart. Blood from the lungs is returned to the heart in the pulmonary veins, and from the rest of the body in the superior and inferior vena cavae.

The cardiac cycle, which averages 833 milliseconds is composed of a period of muscle relaxation called diastole (555 milliseconds) followed by a period of muscle contraction called systole (278 milliseconds).<sup>1</sup> The ventricles are filled with blood during diastole and expel the blood during systole. The atria and ventricles do not contract simultaneously. The atria contract first, filling the relaxed ventricles and then relax while the ventricles contract.

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<sup>1</sup>Unless as noted to the contrary, all cardiovascular data will apply to the human.

The heart, to ensure unidirectional blood flow, has four valves: mitral, tricuspid, aortic, and pulmonary. Figure 2 shows in block diagram form the four heart chambers, the body and lungs, and the four heart valves (each represented by an ideal electrical diode). The mitral (or bicuspid) and tricuspid valves, which are the left and right atrioventricular (AV) valves, respectively, prevent backflow of blood from the ventricles to the atria during systole. The aortic and pulmonary valves, which are the left and right semilunar valves, respectively, prevent backflow from the aorta and pulmonary artery into the ventricles during diastole. The AV valves are open during diastole and the semilunar valves are open during systole. It is supposed that these valves open and close passively with their action depending only upon the pressure gradient across them and not on any intrinsic muscles connected to the valves themselves (123).

When the ventricles contract, they do not empty completely. The amount of blood remaining in each ventricle is called the end-systolic volume and it averages 80 milliliters. During diastole each ventricle fills to an average volume of 150 milliliters -- this is called the end-diastolic volume. The amount of blood ejected with each heart beat is the difference between the end-diastolic and end-systolic volumes and is called the stroke volume. It averages 70 milliliters for each ventricle.

The amount of blood pumped by the heart each minute is called the cardiac output and in a resting, normal 70 kilogram adult averages almost 5.0 liters per minute. The cardiac output is obviously equal to the stroke volume in liters times the heart rate in beats per minute. This very important relationship when carried over to the design of an artificial pumping device shows that two main methods are available to alter the fluid output of the pump.

Blood pressure is the force exerted by the blood against any unit area of the vessel wall. It can be measured in dynes per square centimeter or, more customarily, in millimeters of mercury (mm. Hg). The conversion between the two is:  $1 \text{ mm. Hg} = 1,333 \text{ dynes per square centimeter}$ .

When the left ventricle empties, the normal peak aortic pressure (or systolic pressure) is 120 mm. Hg. This ejection of blood into the arterial system causes the arterial walls to stretch and raises the pressure in the arterial system. After the aortic valve is closed, the aortic pressure falls slowly throughout diastole. This pressure, in the normal human being, usually falls to approximately 80 mm. Hg (diastolic pressure) by the time the ventricle contracts again. The difference between the aortic systolic and diastolic pressures is called the pulse pressure and it averages 40 mm. Hg. The pressures in the pulmonary artery are similar in shape to those in the aorta only with lower systolic (approximately 22 mm. Hg),

diastolic (approximately eight mm. Hg), and pulse (approximately 14 mm. Hg) pressures.

The actual blood pressure at any point in the circulatory system is determined by several factors: 1) the amount of blood in the circulatory system; 2) the pumping activity of the heart; 3) a vessel's resistance to blood flow; and 4) blood density and viscosity.

Another term which will be of importance later is the mean circulatory pressure (MCP). This is the pressure that would be measured in the circulation if one could instantaneously stop all blood flow and could bring all the pressures in the circulation immediately to equilibrium. This value has been found to be almost exactly seven mm. Hg (51). The importance of the mean circulatory pressure is that it is one of the major factors that determines the rate at which blood flows from the vascular tree into the right atrium of the heart, and, therefore, helps to control the cardiac output itself.

The heart derives its rich blood supply from the right and left coronary arteries which arise from the base of the aorta just above the aortic valve. Blood returning from the tissues of the heart itself flows through the coronary sinus into the right atrium or returns by a number of smaller vessels to the atria and ventricles.

The average weight of the normal adult heart is about 312 grams in the male and 255 grams in the female. Its

approximate dimensions are: length, 12.7 centimeters; width, 8.9 centimeters; and depth, 6.35 centimeters. The adult heart is about 1/300 of the body weight (123).

The main mass of the heart is formed by its muscular tissue or myocardium, lined internally by endocardium and externally by the pericardial tissue layer known as epicardium. In addition, there are blood and lymphatic vessels, nerves, varying amounts of fat and areolar tissue, and specialized conducting tissues.

The heart is composed of three types of cardiac muscle: atrial muscle, ventricular muscle, and Purkinje muscle fibers. The atrial and ventricular muscles act in a manner similar to skeletal muscle, while the Purkinje fibers provide a rapid transmission path for the conduction of impulses.

The heart-beat commences in the sinoatrial node located on the right atrium. This node is called the pacemaker of the heart and its fibers have a natural rate of about 70 impulses per minute. From the sinoatrial node the impulses pass through the atrial wall, to reach the smaller atrioventricular node. This node directly continues into the atrioventricular bundle (bundle of His) which provides a single conducting pathway between the two masses of contractile tissue.

The bundle of His delivers the impulses to the ventricular septum wherein the pathway divides to form the



right and left bundle branches. These branches carry the impulses to the entire endocardial surface of each ventricle.

When an action potential occurs in cardiac muscle, the muscle continues to contract as long as the membrane remains depolarized. When the heart rate is increased the duration of contraction decreases almost as much as the rate increases. Thus the ratio of systole to diastole remains nearly constant at 1:2.

The nerve supply of the heart is derived from the autonomic nervous system, and contains both sympathetic and parasympathetic elements which are antagonistic in function. The parasympathetic nerves (the vagi) innervate the atrial musculature very strongly. Acetylcholine secreted at the vagal endings has two major effects on the heart: 1) it decreases the rate of rhythm of the sinoatrial node and 2) it slows the transmission of impulses into the ventricles. The sympathetic nerves are supplied to all areas of both the atria and the ventricles. Sympathetic stimulation increases the overall activity of the heart in three ways: 1) it increases the rate of the sinoatrial node, 2) it increases greatly the force of contraction of all the cardiac musculature, and 3) it increases the excitability of all portions of the heart.

The dynamic behavior of the vascular system itself can also be significantly regulated by neurogenic control. Sympathetic stimulation, causing a concurrent increase in

the smooth muscle tone of the vascular walls, increases the pressure at each point in an artery or vein. The opposite situation occurs with sympathetic inhibition.

Two types of changes in the heart are related to respiration. The first is the mechanical displacement and change in state accompanying the movements of the diaphragm. The second change depends upon the indirect effect of altered intrathoracic pressure. Forced expiration against resistance raises the pressure in the thorax to a level above that of the blood in the extrathoracic veins, and the latter become distended with blood which is unable to return to the thorax. As a result of the diminished venous return, the heart shows an appreciable diminution in volume and output. Inspiration, especially forced inspiration against resistance, has the opposite effect and usually causes a sudden increase in cardiac volume and output.

The mechanical work output of the heart is the amount of energy that the heart transfers to the blood while pumping the blood into the arteries. Energy is expended to create both potential energy of pressure and kinetic energy of blood flow. According to Guyton (51), the work output required to create the kinetic energy is less than one percent of the total work output of the heart. The power requirement of the heart is about 0.005 horsepower and the energy for this power is derived mainly from the metabolism of glucose (51). Most of this energy is converted

into heat and a much smaller portion into mechanical work. The efficiency of the normal heart beating under a normal load is around five to ten percent.

#### Cardiac Output and Venous Return

Cardiac output is perhaps the single most important variable of the entire circulatory system, for it provides blood flow through all the individual organs and tissues. Cardiac output is considered to be the output of blood from the left ventricle into the aorta while venous return is considered to be the flow of blood from all the systemic veins into the right side of the heart. Cardiac output must be equal to the venous return over any extended period of time.

Basically, cardiac output is a function of the heart itself, and any factor that changes the effectiveness of the heart as a pump also alters cardiac output. Pathologic factors can affect the pumping action of the heart as can changes in the pressure surrounding the heart resulting from opening the chest.

The two basic means by which the heart can regulate its pumping action and thus its volume output are, first, by changing the heart rate and, second, by changing the stroke volume.

Obviously any increase in heart rate, if the stroke volume remains constant, causes a proportional increase in

cardiac output. Thus, any means for regulating the heart rate is also a means for regulating the cardiac output. As was mentioned previously, the heart rate, aside from its basic intrinsic rhythm, is controlled mainly by the autonomic nervous system. Vagal (parasympathetic) stimulation decreases the heart rate while sympathetic stimulation increases it. The upper limit of the heart rate for effectively increasing the cardiac output is about 200 beats per minute. Above this rate ventricular filling is severely compromised because of a very short diastolic filling period.

To understand the regulation of cardiac output by changing the stroke volume, an intrinsic ability of the heart to adapt itself to increasing loads of inflowing blood should first be noted. This is called Starling's Law of the Heart (114). This law states that the greater the heart is filled during diastole, the greater will be the force of cardiac contraction and consequently the greater will be the quantity of blood pumped. This law can also be stated: within physiologic limits, the heart pumps all the blood that comes to it without allowing an excessive rise in venous pressure. This law forms the basis of the automatic control system developed in this study.

Starling's Law can be graphically depicted as is shown in Figure 3. These curves are called ventricular function

curves and they illustrate that the greater the volume of blood in each ventricle immediately before contraction, the greater also will be the stroke volume (51). Now the regulation of cardiac output by means of changing the stroke volume can be more fully discussed. The middle curve in Figure 3 applies only for a constant degree of cardiac contractility (the vigor with which the heart muscle contracts). The most important factor that can change cardiac contractility is stimulation of the heart by the sympathetic nervous system. The figure shows that sympathetic stimulation increases the stroke volume at each level of ventricular filling, while sympathetic inhibition decreases the stroke volume at each level of filling. The importance of this neurogenic regulation of cardiac contractility is that it provides a means for controlling cardiac output separately and independently from the control of heart rate.

#### The Effects of Right Atrial Pressure On Cardiac Output

Since both ventricles obey Starling's Law, the study of the effects of atrial (or filling) pressure on cardiac output is very important. It is this pressure which was chosen as the controlling parameter to regulate the fluid output of the artificial ventricles developed in this study.

Within normal physiologic limits, increasing the right atrial pressure increases the amount of blood that flows

from the right atrium to the right ventricle and consequently also increases the amount of blood pumped by the heart. The effects of right atrial pressure on cardiac output can be expressed in graphical form as is shown in Figure 4. These curves are called a family of cardiac output curves. It can be seen from the figure that the fluid output of the heart, whether the heart be normal, weakened, or strengthened, is highly dependent upon the right atrial pressure.

The effect of opening the chest on cardiac output should be noted. The set of cardiac output curves applicable to this open-chest situation would be similar to those of Figure 4 except that right atrial pressures would now be about four mm. Hg greater in each instance for the previous level of cardiac output. Unfortunately when the chest is opened, the right atrial pressure usually does not become sufficiently enhanced to maintain normal filling of the heart, and the heart may fail to pump adequate quantities of blood.

The three most important factors that affect venous return are 1) right atrial pressure, 2) mean circulatory pressure, and 3) resistance to blood flow through the systemic vessels.

The normal right atrial pressure is approximately zero mm. Hg in relation to the atmospheric pressure. At this level the venous return is five liters per minute under

resting conditions. Figure 5, which is called the normal venous return curve, illustrates the effects of right atrial pressure on venous return when the circulatory reflexes have been completely blocked. Two portions of this curve should be explained:

- 1) The level to which venous return can increase is the plateau caused by venous collapse at negative right atrial pressures.
- 2) The venous return is directly proportional to the difference between the mean circulatory pressure (MCP) and the right atrial pressure (RAP) until the plateau is reached. Altering the mean circulatory pressure affects the venous return curve by causing only a vertical displacement from the normal curve. The shape of the curve remains unchanged. Also, since venous return can never be negative, the upper limit to which right atrial pressure can rise is equal to the mean circulatory pressure.

Figure 6 illustrates the effects on the venous return curve of changing the systemic resistance. (Systemic resistance is the opposition to blood flow.) Venous return still becomes zero when the right atrial pressure rises to reach the mean circulatory pressure. Since the veins have a larger blood volume than do the arteries, the resistance from the veins to the heart has much more effect

on venous return than does arterial and capillary resistance.

Except for a few seconds at a time when blood is actually being accumulated or lost from the lungs or heart, venous return must equal cardiac output. Figure 7 shows the normal cardiac output curve superimposed upon the normal venous return curve. It can be seen that venous return and cardiac output equal each other.

When an attempt is made to analyze the effect of some change on cardiac output, the effect that the change will have both on the ability of the heart to pump and also on the venous return must be considered. Then these changes must be evaluated together to determine the final effect on cardiac output.

The effect of sympathetic stimulation on cardiac output will be briefly noted. Sympathetic stimulation strengthens the heart and thus increases its ability to pump blood. Also, sympathetic stimulation augments venous return by principally increasing the mean circulatory pressure and slightly increasing the resistance to venous return. The combination of these two effects is shown in Figure 8 where moderate and maximum sympathetic stimulation are contrasted with the normal action. Points A, B, and C show, respectively, the equilibrium points for increasing sympathetic stimulation.



Other physiologic states, such as exercise, transfusion, fever, and opening the chest, can be similarly analyzed. Thus a large number of different factors can cause acute (short-term) changes in cardiac output. However, the most important factor that determines cardiac output is probably the need of the tissues for oxygen. Oxygen utilization, then, constitutes a means of long-term regulation of cardiac output.

#### The Function of the Veins

The veins, once thought to be only passageways for the flow of blood to the heart, are capable of constricting and enlarging, storage of blood, propelling blood forward, and even helping to regulate cardiac output.

The pressure in the right atrium is also called the central venous pressure. Right atrial pressure is regulated by a balance between, first, the ability of the heart to pump blood and, second, the tendency for blood to flow from the peripheral vessels back to the heart. This latter effect is a function of blood volume, venous tone, venous pressure gradient, and by dilation of the systemic small vessels. The normal right atrial pressure is approximately zero mm. Hg but can change in various pathologic states from -4 mm. Hg to as high as +20 mm. Hg.

The large veins have almost no resistance when they

are distended. Since this is not normally the case, the large veins usually do offer considerable resistance to blood flow. Thus pressures in the peripheral veins are usually six to nine mm. Hg greater than the right atrial pressure. When the right atrial pressure rises above its normal value, blood begins to accumulate in the large veins thus distending them. However, the pressures in the peripheral veins do not rise until all the collapsed points between the peripheral veins and the large veins have opened up.

Hydrostatic pressure affects the values of venous pressure in the peripheral veins, from a value of +90 mm. Hg in the feet to -10 mm. Hg in the sagittal sinus of the head. However, the right atrial pressure still remains approximately at its normal value. The veins have small one-way valves in them that help in moving the blood centrally. These valves are passive and are activated by the flowing venous blood. This venous pump is so efficient that, under ordinary circumstances, the venous pressure in the feet of a walking adult is less than +30 mm. Hg.

Physiologically, there is one point in the circulatory system at which hydrostatic pressure does not affect the blood pressure measurement by more than one mm. Hg. This point is at the level of the tricuspid valve as is shown in Figure 9. Therefore all pressure measurements are referred to this level which is called the reference point

for pressure measurement. The reason for the lack of hydrostatic effects at the tricuspid valve is that the heart automatically prevents any significant variation in pressure at this point by appropriate changes in its cardiac output and filling capacity. In venous pressure measurements the reference level must be very exact if the measurements are to be significant; for very small variations in venous pressure result in great changes in cardiac output.

Approximately 50 percent of all the blood in the circulatory system is in the systemic veins (51). Thus the veins act as a blood reservoir for the circulation. An extremely important function of this venous reservoir is its ability to change both its volume and the rate at which blood is returned from the peripheral vessels to the heart. Sympathetic stimulation of the venous reservoir, for instance, can elevate venous return and cardiac output up to as much as two and one-half times normal. Increased venous return due solely to venoconstriction, however, terminates when excess volume is transmitted to the heart. Then the effects of increased cardiac output through the system maintain the elevated flow rate.

#### Regulation of Arterial Pressure

The arterial pressure is normally regulated at a level much higher than is needed to provide normal blood flow to

the tissues. This allows the tissues to suddenly increase their blood flow by locally dilating their arterioles. The systolic pressure of a normal young adult averages about 120 mm. Hg, while the diastolic pressure averages about 80 mm. Hg. The mean arterial pressure is the average pressure throughout the cardiac cycle and it averages about 96 mm. Hg.

An analog can be made for the pressure-flow characteristics of a vascular area by using the voltage-current relationship of an electrical resistor. The voltage drop across the resistor equals the current through the resistor times the resistance. For the entire body then, blood pressure equals cardiac output times total peripheral resistance. Thus the body can control its mean arterial pressure by changing either the cardiac output or the total peripheral resistance. One of the most important functions of the arterioles in the circulation is the regulation of peripheral resistance.

There are three chief methods by which the arterial pressure is normally regulated. Each method operates at least partially independently of the other two and each has specific capabilities for keeping the arterial pressure regulated at a constant value. These methods are the following:

- 1) regulation by the autonomic nervous system
- 2) regulation by the kidneys
- 3) regulation by the endocrine glands.

The nervous system is extremely important in regulating arterial pressure in the head and in conditions of sudden crises. This method is fast acting but tends to adapt and thus its usefulness in long-term regulation of arterial pressure is limited. Renal regulation of arterial pressure, which includes a capillary fluid-shift mechanism, is slow to react but maintains almost constant arterial pressure. Renal regulation is the best long-term control mechanism. The endocrine glands also constitute a means of long-term regulation of arterial pressure. The action of the endocrine system is complementary to the actions of both the nervous system and the renal system.

The operating features of these three methods are discussed in Guyton (52). It should be obvious that these methods are extracardiac and thus still should be active with an artificial heart in place.

Several other factors concerned with the control of mean arterial pressure by the nervous system should be mentioned. The intensity of sympathetic activity of the vasomotor center in the brain increases almost directly in proportion to the concentration of carbon dioxide in the extracellular fluids bathing this center. Thus, carbon dioxide is one of the most powerful of all stimuli affecting the activity of the vasomotor center which, in turn, affects the arterial pressure.

Respiratory modulation of the arterial pressure is a less important circulatory reflex. The modulation is caused both neurogenically and by mechanical actions of the lungs and diaphragm.

### Blood Volume

The average blood volume of a 70 kilogram adult is 5,000 milliliters. Approximately 2,750 milliliters of this blood is plasma, and the remainder, 2,250 milliliters, is red blood cells. The percentage of red blood cells in the blood is called the packed cell volume (PCV) and is normally 40 for a man and 36 for a woman.

The percentage of the total blood volume in each portion of the circulatory system is (51):

Large veins . . . . .	25
Small veins, venules, and venous sinuses . . . . .	25
Heart . . . . .	18
Pulmonary vessels . . . . .	12
Large arteries . . . . .	8
Small arteries . . . . .	5
Arterioles . . . . .	2
Capillaries . . . . .	5

The term vascular capacity is used very loosely to mean the amount of blood that the circulatory system will hold. Since the mean circulatory pressure is somewhat

proportional to the ratio of blood volume to vascular capacity, it can be seen that the volume must be precisely regulated so that it will always fill the circulatory system up to approximately the same constant pressure.

The compliance of the circulatory system is the change in blood volume that can be accommodated in the circulatory system for each unit change in pressure. From pressure-volume curves of circulatory systems it can be shown that the relationship between blood volume and mean circulatory pressure (MCP) is

$$\text{Blood Volume} = V_0 + (\text{MCP}) (dv/dp)$$

where  $V_0$  is the blood volume of the circulatory system when MCP is zero and  $(dv/dp)$  is the compliance of the circulatory system (52).

The blood volume is regulated by several different mechanisms, each one having its own special capabilities. The plasma volume can increase and decrease markedly in very short periods of time to regulate the blood volume in accordance with the needs of the circulatory system. A capillary fluid-shift mechanism allows relatively rapid loss of fluid from the circulation into the interstitial fluid whenever the blood volume becomes too great. However this mechanism does not return the blood volume all the way back to normal. The final volume adjustment is caused principally by kidney action. This renal mechanism

may require a day or more for blood volume adjustment, in comparison with minutes to hours for the capillary fluid-shift mechanism.

The total volume of red blood cells is very slow to change. The red blood cell volume is regulated almost entirely independently of the total blood volume. The volume of cells is regulated primarily to provide adequate oxygen transport to the tissues. The plasma volume is then adjusted accordingly to finish filling the circulatory system.

#### The Pulmonary Circulation

A minute quantity of blood flows through the bronchial arteries and returns to the left atrium instead of to the right atrium. Thus 1) the quantity of blood flowing through the lungs is greater than that flowing through the systemic circulation and 2) the quantity of blood flowing through the left side of the heart is greater than that flowing through the right side. The difference in flow amounts to, on the average, about one percent (51).

The pulmonary arteries and veins are all very short and do not accommodate nearly so much blood as do their counterparts in the systemic circulation. The blood in the pulmonary arteries is venous blood and that in the pulmonary veins is arterial blood.



The mean pulmonary arterial pressure averages approximately 13 mm. Hg in the normal human while the pulse pressure averages approximately 14 mm. Hg. The mean pressure in the left atrium and in the major pulmonary veins averages approximately four mm. Hg. Thus the normal pressure gradient between the mean pulmonary arterial pressure and the left atrial pressure is nine mm. Hg. When the left atrial pressure rises, the pulmonary arterial pressure also rises almost an equal amount with the pressure gradient falling only slightly. The right ventricle is able to compensate for the increased load. Variations in nervous activity also often aid the right ventricle in load compensation.

The cardiac output can increase to three to four times normal before the pulmonary arterial pressure begins to rise markedly. This is caused by the fact that the pulmonary vessels are normally partially collapsed and can easily tolerate large increases of flow rate. This mechanism conserves much energy if both the blood flow and rate of gaseous exchange must increase suddenly.

The quantity of blood that flows through the lungs is controlled almost entirely by the pumping ability of the heart and by the return of blood to the heart from the systemic circulation. The pulmonary vessels are mainly passive tubes. However, the larger arteries of the pulmonary system are supplied with smooth muscle weakly innervated

by both cholinergic vagal nerve fibers and adrenergic sympathetic fibers. This innervation is responsible for very minor vasomotor reactions which can occur in the lungs.

The blood volume in all the vessels of the two lungs is approximately 600 to 800 milliliters in the average human (51). Under different physiologic conditions, the quantity of blood in the lungs can vary from about 50 percent of normal up to 100 percent or more greater than normal. Since the volume of the systemic circulation is about seven times greater than the volume of the pulmonary circulation, the shift of blood from one circulation to the other affects the lungs greatly but usually has only mild systemic effects.

#### The Coronary Circulation

In the human, the left coronary artery supplies mainly the left ventricle and the right coronary artery supplies mainly the right ventricle. Most of the venous blood from the left ventricle leaves by way of the coronary sinus and most of the venous blood from the right ventricle flows through the small anterior cardiac veins which empty directly into the right atrium.

The coronary blood flow is approximately four percent of the total cardiac output. In humans this is about 225 milliliters per minute. The blood flow rate through the

capillaries supplied by the left coronary artery falls to a very low value after the first third of systole is over. Then during diastole, the cardiac muscle relaxes completely and no longer obstructs the flow of blood through the capillaries. Therefore, blood flows very rapidly throughout most of diastole.

Blood flow through the coronary circulation is regulated almost entirely by a local mechanism in the heart in response to the needs of the cardiac musculature for oxygen. This mechanism works equally as well whether the nerves to the heart are intact or removed. It is believed that oxygen lack dilates the coronary arteries to increase the coronary flow rate (52). However, stimulation of the sympathetic nerves to the heart can increase coronary blood flow several times, while parasympathetic stimulation can decrease coronary flow by perhaps 20 to 50 percent. Yet, it is believed that these results occur secondarily to other effects of nerve stimulation.

## REVIEW OF THE LITERATURE

## Ideal Specifications

A substitute for the natural heart must simultaneously satisfy a combination of difficult requirements. Naturally most of the requirements are fundamental to normal heart action.

Some properties mechanically mimic the normal heart.

- 1) Blood should progress in one direction only.
- 2) Blood should be expelled by a squeezing motion in order to minimize blood trauma.
- 3) The systolic residue (end-systolic blood volume) should remain in the central lumen in order to minimize turbulence.
- 4) Circulatory stasis (stagnation) should be avoided in order to prevent clotting.
- 5) The pump should function quietly and reliably for long periods of time.

The following properties physiologically mimic the normal heart.

- 6) The prosthesis should be an effective hemodynamic support for the circulation by being capable of providing a cardiac output adequate to meet the metabolic demands created by a reasonable level of activity.

- 7) The prosthesis should preferably respond to the physiologic control mechanisms which normally maintain hemodynamic equilibrium.
- 8) The pump should include automatic control of cardiac output to be responsive to the body's demands for blood.
- 9) The flow rate should be adjustable from zero to at least five liters per minute (44).
- 10) The pump should not have a fixed stroke volume.
- 11) The pump should fill even at low negative pressures.
- 12) For adequate filling diastole should be longer than systole.
- 13) The pump should maintain adequate perfusion pressure at no expense to venous pressure (54).
- 14) The mechanism should produce pulsatile flow and should be capable of being adjusted in pulse rate and stroke volume independently (44).
- 15) The presence of the pump should not interfere with the body's normal physiology or activities and should in no way compromise remaining cardiac functions.

The problems of tissue reaction, blood trauma, and clotting must be reckoned with. Selecting the proper materials is extremely important.

- 16) The rate of hemolysis produced by the prosthesis must not only be within the body's capability for

removing the products of hemolysis, but also below the rate of cell destruction which will give rise to a progressive anemia, i.e., the blood constituents should be destroyed at rates smaller than those which characterize their production (16).

- 17) The pump should be compatible with other body tissues and should not provoke the hazards of infection and tissue reaction.
- 18) Local turbulence in entrance and exit zones and around necessary valves, branches, and other constrictions should be minimized.
- 19) The pump should have minimal chances of immediate or latent hemorrhage.
- 20) The pump should require no heparin or other anticoagulants while functioning -- at least to the point that normal clotting mechanisms would not be significantly altered (54).
- 21) The materials used and the geometric design chosen must be such as to minimize the tendency toward clot formation.
- 22) There should be minimal contact of blood with foreign materials and the blood containing components should be smooth and nonwetable.
- 23) Surfaces in contact with blood should not touch or occlude during operation (1).

- 24) The pump should be fabricated of strong and durable material -- rigid material should be avoided where possible (54).
- 25) Stress in all moving parts should be minimal and uniform (1).

Factors such as size and weight, power and efficiency, and costs of both manufacture and operation must be considered.

- 26) The pump should have space and design requirements which would not compromise adjacent organ structures.
- 27) The pump should be lightweight.
- 28) The pump should operate at relatively high efficiency in order to minimize the power requirements and thus make operation independent of fixed power sources.
- 29) In the event of any power failure, the unit should be capable of manual operation.
- 30) There should be minimal heat production by the artificial pump.
- 31) The design should lend itself to standard fabrication techniques so that many units could be built without extensive tooling and yet retain as much flexibility for design changes as possible.
- 32) Initial cost should be reasonable and maintenance cost low.

Finally, installation, operation, and safety must be taken into account.

- 33) There should be a reasonably simple surgical procedure for insertion in as short a time as possible.
- 34) There should be a physiologic access plug to facilitate connection of the pump to an extracorporeal power and control system.
- 35) Pumping adjustments should be simple to make and settings should remain fixed for uniform performance.
- 36) The system should possibly allow for pumping synchronization with the variable atrial rate, uninfluenced by both movement due to physiologic processes and electrical interference from the outside (91).
- 37) The pump should be completely safe to use -- it should not jam, skip beats, burst, or leak.
- 38) The unit should be so designed that malfunctioning could be quickly detected, diagnosed, and possibly corrected.

If a majority of these conditions are realized, it is very probable that individuals with such prostheses could engage in reasonably normal social activity and occupation.

#### Types of Pumps Developed

A variety of pumps have been used with various types of oxygenators in extracorporeal circulation units. Many



of these pump designs have been carried over into the development of intrathoracic artificial hearts. The pumps most frequently used have been the roller, the finger, and the diaphragm type. The dual-roller blood pump continues to be employed in most extracorporeal blood circuits despite the fact that a number of pumps have been designed that are capable of propelling blood with less trauma (44). Pumps which are less traumatic usually consist of ventricles which are compressed externally by hydraulic or pneumatic force.

The operation of a roller-type pump is quite simple. A flexible tube carrying the fluid to be pumped is secured in a circular frame. A rolling cylinder moves along the tube thus squeezing the tube between the cylinder and the frame. This moving occlusion then pushes the fluid through the tube. With regard to the advantages of one versus two (or more) rollers in a blood pump, it has been shown that increasing the number of rollers and therefore reducing the stroke volume increases hemolysis for a given volume of blood pumped (43). Esmond et al. (44) developed a single-roller blood pump which used the minimum force needed to just occlude the tubing. This pump produced very low hemolysis rates but was intended for extracorporeal use only.

Pierson et al. (101) investigated the use of a small lightweight roller pump to achieve acceptably low hemolysis rates. Their high speed, partially occlusive pump operated

at outputs in the range of two liters per minute.

The shortcomings of roller pumps and of conventional round tubing for long-term blood pumping are interrelated. Relatively high degrees of occlusion and/or high speed are required in order to minimize backflow. Backflow tends to produce turbulence which in turn induces hemolysis. Also, appreciable hysteretic power losses are inherent with a round cross-section because of the high deformation accompanying the 85 to 100 percent occlusion usually required.

A pump and tubing device has been designed which combines certain advantages of valved pumps with the structural and operational simplicity of roller pumps (100). The principal design innovation in this low-powered and readily-miniaturized pump was the use of flat rubber tubing whose interior was segmented into small chambers by thin leaflet bicuspid valves. Backflow was avoided and relatively high volumetric pumping efficiencies were obtained at low degrees of occlusion. This design represented efficient use of input power.

The fluid-actuated heart pump has seen little use in extracorporeal pumping circuits. However it is still a very popular type of pump because of its use in many artificial heart designs. It is characterized by low weight, high reliability, low heat production, and low hemolysis (59). The outstanding feature of such a pump, with an external

control system, is that great flexibility of operation is possible without any adjustments of intrathoracic components.

A fluid-actuated artificial heart pump is shown schematically in Figure 10. If the controlled actuating fluid pressure  $P_C$  is reduced to a value lower than the venous return pressure  $P_R$ , the moving element (rolling or stretched diaphragm, collapsing bag, or reciprocating piston) will travel to the left. The inlet valve will open and a volume of blood will be accepted by the pump. If  $P_C$  is then increased to a value greater than the arterial pressure  $P_A$ , the moving element will travel to the right. This action closes the inlet valve, opens the outlet valve, and forces the volume of blood into the arterial system. Causing  $P_C$  to pulsate according to some repetitive waveform will permit continued pumping of the heart.

Both air- and liquid-actuated hearts have been built, with the former type being the most popular. Hastings et al. (56, 57) pursued the development of a liquid-driven artificial heart. They devised a two-chambered, hydraulically-activated diaphragm pump.

The Cleveland Clinic's Department of Artificial Organs has been very instrumental in the development of air-driven artificial hearts. The fabrication, testing, use, and control of their artificial pumps have been well documented. Important publications by this group are the ones directly concerned with air-driven artificial hearts ( 4, 5, 6, 88,

92, 94, 110, 111), those dealing with methods of power and control (58, 59, 66, 96), and finally those discussing the testing and the damaging tendencies of their various pumps (23, 29, 39). Several of the Clinic's staff have written excellent treatises on the problems encountered in artificial heart development (63, 64, 89).

Several pumps have been designed to specifically overcome certain inherent problems common to most artificial hearts. One of the problems is that of suction which is not a normal feature which aids in ventricular filling during diastole. Under normal conditions, about one-half of the stroke volume enters the ventricle at the beginning of diastole. The area of the mitral valve shifts upward and "engulfs" the blood that has accumulated in the atrium during ventricular systole. To prevent suction from occurring, a rather large sliding pump that duplicated this engulfing action was devised (103). Another way to obtain an adequate stroke volume with minimal suction in a diaphragm-type pump is to make the pump flat and thus have a large membrane area. Using this idea, Liotta et al. (79) developed a membrane-type pump in which systolic residue, filling time, and the amount of suction pressure were easily controlled.

A second and more serious problem inherent in any blood pumping device is that of hemolysis. In an attempt to alleviate this problem, an unconventional artificial heart

using only a single ventricle was developed (99). In this system a biologic circulatory bypass replaced the right ventricle and thus eliminated one pump. The system's main features were its advantages over the conventional two-ventricle artificial hearts -- less blood damage, fewer valves, smaller size, greater reliability, and decreased energy requirements.

A rather novel artificial heart employed a flexing piezoelectric crystal (80). The use of this material permitted a direct and efficient conversion of electrical energy to pumping energy.

Second in popularity to fluid-driven artificial hearts are those hearts which use small integral motors to provide the pumping power. Their main advantage is in their controllability in that the fluid output is almost directly proportional to motor speed. Houston et al. (60) developed an a-c motor-driven two-ventricle artificial heart. The motor, through a gear reduction system and a set of pivots and eccentrics, swung back and forth within a rigid housing. The body of the motor alternately compressed each ventricle against the housing thus expelling its contents. This pump exhibited both low hemolysis and some degree of automatic regulation via atrial pressure changes.

Akutsu et al. (3) developed a similar d-c motor-driven heart in which the motor drove a small freely moving roller. The roller rotated within a brass housing in which there

were two polyurethane ventricles. The ventricles pumped alternately. This pump also showed low hemolysis and some degree of automatic regulation.

The extracorporeal roller pump is not without its miniaturized intrathoracic equivalent (101). Small motor-driven piston-type blood pumps have also been built (24, 62, 97). A flat pancake-type d-c motor was built into the base of a piston pump (99). A set of cams and gears converted the rotary motion to pulsatile motion. This motor consumed very little power -- 10 watts.

A variation of the piston-type pump, developed by Burns et al. (28), was versatile in that both the pulse rate and the pressure waveform could be varied independently. This same group later reported on the development of another motorized heart in which the motor provided power to an hydraulic fluid (27). The fluid, when properly controlled by internal valves, did the pumping work.

The electromagnetic solenoid has also been employed to actuate the moving element of an artificial heart. Kolff (65) utilized several small solenoids in his initial artificial hearts.

#### Materials

The choice of materials for a mechanical heart is based on a number of factors, but prime consideration is given to

long mechanical life and non-destruction of the blood elements.

Consideration of the problem of long-term survival with an artificial heart indicates that one of the primary problems to be solved is the prevention of clot formation either in the prosthesis or in a natural vessel of the body. Sawyer (105) has stated that efforts dedicated to the fabrication of mechanical blood pumps will be unsuccessful until there is made available a plastic which reacts to blood as does the normal vascular intima.

Pumping blood with a mechanical, implantable device made of impervious plastics invariably leads to the deposition of a blood protein onto the luminal surfaces of the device. Such a deposition has been observed on many useful plastics, such as methylmethacrylate, polyurethane, silicone rubber, lucite, teflon, and silk (79). Liotta et al. (74) have found that soon after such pumps begin functioning, the unattached film of blood protein, which varies in thickness, is observed on the luminal surfaces of both the inlet connectors and the blood chamber. Later it appears disintegrated and accumulated at valves or embolized into the arterial system. The propensity for thrombus formation is not identical in all animals. It is generally agreed that the problem of thrombosis on a prosthesis is much more severe in the canine heart than in the human heart (48).

Considerable research has been carried out by a number

of investigators on the relation between blood coagulation and the material in immediate contact with the blood. Gott et al. (49) have been able to obtain an antithrombogenic surface using a graphite-benzalkonium chloride-heparin coating.

Velour fabric was found to be an excellent blood-contacting surface (74). The velour-type liner fosters development of a strong, permanent mechanical bond between the plastic and the internal fibrin lining. Trapped and held, this coagulum forms an autologous lining within the pump, protecting the blood from further contact with the foreign material. Once this formation has been achieved, the blood-plastic interface within the mechanical pumping system no longer exists and chances of dissection and embolization are negligible.

Liotta et al. (74) have been instrumental in the use of this material and have achieved rewarding results. They reported that, during pumping, plasma hemoglobin levels fell to preoperative values and a prolonged patency of the mechanical system was achieved. They found that pumps lined with nylon velour fabrics demonstrated the best fibrin attachment and dacron velour was second. They stressed, however, that a satisfactory pseudoendocardium could be obtained only if the pumping chamber was properly designed, the valves were so placed so as to eliminate areas of stagnation, and a high hemodynamic condition was maintained throughout the



mechanical pumping system. They also emphasized that the mechanical characteristics of a material were as important as its chemical composition.

The main mass of most artificial hearts has been fabricated from lucite, silicone rubber, or natural latex rubber. The majority of these have used a medical grade of silicone rubber which has usually been reinforced with a woven material. Silicone rubber is a synthetic material which is minimally reactive when in prolonged contact with blood.

Size and weight factors can also influence the choice of materials. A comparison has been made on a weight basis of normal and artificial hearts. If the normal heart weighs 400 grams, then a natural rubber artificial heart with the same pumping capacity weighs 350 grams; a silicone rubber heart, 650 grams; and a fluid amplifier heart, 800 grams (92).

#### Artificial Valves

Artificial heart pumps, which function by the intermittent compression of a chamber by air or fluid require valves in the inflow and outflow tracts to ensure unidirectional flow.

The valve designs used in artificial hearts are mainly outgrowths of the various types of valves used in replacing diseased heart valves in humans. The two most common ones

are the ball valve and the flap or leaflet valve. Valves made with cusps and other types which physically duplicate the actual heart valves have also been used.

Cartwright et al. (32) give a short history of the development and use of ball valves along with a description of a newer ball valve of their own design. Because of relatively large size requirements, ball valves have been used less and less in the later artificial heart designs. Leaflet valves are smaller and lighter in weight, operate with less mechanical movement and pressure gradient, and are less sensitive to gravity effects than are ball valves. Thus their use is becoming more prevalent not only in artificial hearts but also in human hearts with malfunctional valves.

The formation of thrombi on artificial valves is probably the greatest obstacle to their successful application in artificial hearts, since fibrin deposits are very common on and around the valves. Deposits form rapidly in any stagnant area. Akers et al. (1) have found that the discharge side of leaflet valves in the aortic position quickly develop large fibrin deposits, and that these deposits initiate at any joint or roughness in the surface. Mirkovitch et al. (86) indicated that only plastics with smooth surfaces, suspended in the middle of the blood stream, and without direct or extensive contact with tissue stay free of thrombi. They also set forth some rules for the design of an artificial valve:

- 1) The leaflets of the valve should have a smooth surface.
- 2) The leaflets should be exposed to a strong, moving blood stream.
- 3) No small or motionless pockets filled with stagnant blood and no narrow commissures should be present.
- 4) The valve parts should exhibit minimal friction with each other.

Naturally, the criteria by which the artificial valve is judged are based on how well it approximates a normal, natural valve.

Dreyer et al. (39) give further necessary specifications for valves to be used in artificial hearts:

- 5) The valve should not induce the deposition of fibrin.
- 6) The valve should be atraumatic to the constituents of the blood.
- 7) The valve should be very durable and exhibit a long mechanical life.
- 8) The valve should be completely competent during the closing phase.
- 9) The valve's action should be swift.

A final requirement is that of low forward resistance to the flow of blood. This is especially important on the input side to obtain a sufficient venous return. If the

inflow valve resistance is low the artificial heart will function according to Starling's law (92). But when the inflow resistance is high, the atrial pressure required to fill the ventricle must also be high and suction may be necessary.

Probably the most critical aspect of a flap or leaflet valve is the selection of a satisfactory leaflet material. The valve leaflet has to be very flexible so that it can open with a small pressure gradient and yet have the strength and stiffness so that it can withstand a high back pressure (140 mm. Hg maximum). Gott et al. (48) tested many leaflet materials and found polyvinylfluoride to be the most successful plastic film. They coated some of their plastic surfaces with colloidal graphite and found a very definite reduction in clot formation. Colloidal graphite is extremely non-wettable, conductive, and chemically inert and it is a very smooth surface.

In 1964, Gott et al. (49) described a new type of anti-thrombogenic coating which contained graphite, benzalkonium, and heparin (GBH). The important antithrombogenic property of graphite is that it has the ability to bond firmly a cationic surface agent (benzalkonium), which in turn can bond heparin. They obtained routine long-term survival of dogs with GBH coated prosthetic valves.

Gott et al. (48) have also designed a flap valve constructed of a rigid plastic housing and a flexible

"butterfly-wing" leaflet. This valve was subsequently GBH coated and has become a very popular prosthesis for human heart valves.

Aside from the thrombosis problem, the other major concern in valve design is that of hemolysis (blood cell trauma). Nunn et al. (95) have indicated that diaphragm and other compression-type artificial hearts cause little cell damage. The actual degree of hemolysis is largely dependent upon the type of valves employed. They performed a study to determine the relative amounts of hemolysis caused by three types of valves (flexible tricuspid, "butterfly", and ball) suitable for use in air- or fluid-driven artificial hearts. They established that all valves tested showed a linear increase in plasma hemoglobin production as pumping time increased. Akers et al. (1) found that the rate of hemolysis was almost directly related to the pulse rate and was only slightly affected by flow rate. They showed that leaflet, tricuspid, and soft disk valves had the lowest rates of hemolysis, ball-type valves were intermediate, and hard disk valves were the highest. With regard to backflow, this same study found that it was highest in ball-type valves, intermediate in disk-type valves, and lowest in leaflet and membrane valves.

All artificial valves should be tested in a mock circulatory system to ascertain their performance. Dreyer et al. (39) and Steinmetz et al. (115) describe mechanical

systems to carry out such tests. The latter group has developed an accelerated fatigue machine which can subject a valve to physiologic pressure variations at rates up to 2,500 cycles per minute.

### Blood Trauma

Any serious effort at prolonged mechanical support of the circulation must consider the biologic tolerance to continuing damage imposed by the support system. Such damage includes the immediate breakdown of red blood cells, the presence of the envelopes of the cells in the circulation, and other, more subtle, forms of damage to the blood cells which may impair their ability to survive or function over a normal life span (12). This damage is one obstacle which precludes the continuous use of mechanical circulatory support systems for periods of unlimited duration (70).

Hemolysis, or the separation of the hemoglobin from the corpuscles and its appearance in the fluid in which the corpuscles are suspended, is the usual way of measuring the degree of trauma inflicted by artificial pumps and valves. The presently accepted method of reporting hemolysis is the index of hemolysis (I.H.) (118). This index is determined by the total production of free plasma hemoglobin divided by the number of passages the blood has made through the device:

$$\begin{aligned}
 \text{I.H.} &= \frac{(H_f - H_c) \times 100}{\text{Number of passages}} \\
 &= \frac{(H_f - H_c) \times 100}{FT/V}
 \end{aligned}$$

where  $H_f$  = final plasma hemoglobin (grams per liter)  
 $H_c$  = initial plasma hemoglobin (grams per liter)  
 $F$  = flow rate (liters per minute)  
 $T$  = time (minutes)  
 $V$  = priming volume (liters)

The units on the index of hemolysis are grams of free hemoglobin released per 100 liters of blood pumped. Esmond et al. (44) have stated that the pumping rate and the pressure against which the blood is pumped must be given for this index to have significance.

Wesolowski (118) indicated that repeated passages through a given pump at a given flow led to a linear increase in production of free plasma hemoglobin and thus there was apparently no great summative effect of the same red cell having been traumatized twice by the pump. This suggests that hemolysis may be an all or nothing effect for any particular red cell. This group found that free hemoglobin production was a function of the flow rate whereas Akers et al. (1) indicated it was a function of the pulse rate. However, these two factors are interrelated since flow rate equals cardiac output (liters per beat) times pulse rate

(beats per minute).

In making comparisons between the degree of hemolysis caused by different pumps, the test circuit should be entirely in vitro. The reason that an animal should not be in the circuit is that free hemoglobin is withdrawn from the circulation continuously by the kidneys, liver, and the reticular-endothelial system and the rate of removal varies from animal to animal (117). Therefore, the actual measurement of free hemoglobin in the circulating plasma is not a true measure of the cellular destruction. It has been found that humans, not in a state of dehydration or shock, can clear doses of up to 14 grams of free hemoglobin within 24 hours if they possess normal renal function (12). It should be pointed out that red cell destruction is a normal event in animals. In a 70 kilogram human, blood is destroyed at the average rate of 0.093 milligrams for every 100 milliliters of blood circulated (44).

Plasma hemoglobin measurements, however, do not tell the whole story about trauma to red cells. Kusserow et al. (71) suggested that prolonged circulations with reasonably atraumatic blood pumps resulted not only in the outright or prompt destruction of a certain fraction of the red cells initially present, but also in the infliction of significant damage on other erythrocytes short of outright destruction, followed by premature senescence of the cells and anemia. Since these abnormalities also do not show up



in in vivo tests, in vitro studies of the mechanical fragility of cells are very important (23).

Most prosthesis-development groups have tested their devices for degrees of hemolysis. Pierson et al. (101) stated that fresh heparinized blood should be used within four hours of extraction from an animal for the hemolysis studies. Their small motorized roller pump gave an index of hemolysis of 0.17 to 0.29 with canine blood. Using an improved version of their roller pump, this same group later reported an index of hemolysis of 0.33 with human blood (100). The pumping system devised by Kusserow and Clapp (69) gave an index of hemolysis at a flow rate of 1225 milliliters per minute of 0.08 with fresh heparinized canine blood in a 0.5 liter capacity system. Castañeda, et al. (33) reported an index of hemolysis of 0.08 to 0.18 at flow rates of 1.5 to 3.5 liters per minute with the army heart pump.

#### Other Problems Associated With Artificial Hearts

An artificial heart is a prime example of a homeostasis-maintaining artificial organ which experiences and provides for the flow of blood in it while transferring mechanical energy to the blood. To guarantee its intended purpose, the blood handling must be achieved under atraumatic physical and chemical conditions.

Many artificial blood pumps presently being used are too toxic for prolonged use because they destroy the formed elements in the blood. Leonard (72) stated that the primary cause of mechanical degradation appeared to be shear forces exerted on a particle in a region with a high fluid velocity gradient. However, Salisbury et al. (103) believed that the functional disadvantages were due not only to turbulence but also to negative blood pressure during the filling phase in the pumping chamber and to crushing of blood cells between opposing surfaces.

It appears that there are distinct advantages in having an artificial heart produce a pulsatile blood flow. The evidence suggests that pulsatile flow is important not only in the design of an artificial heart but also during long-term extracorporeal circulation. Burns et al. (28), in a series of tests found that both systemic and pulmonary vascular resistance increased (125 percent and 127 percent, respectively) with non-pulsatile flow as compared to pulsatile flow. Further, they indicated that this resistance change was unaffected by sympathetic or parasympathetic blockade, nephrectomy, or baroreceptor denervation. It is also possible that unphysiologic pressure curves generated by an artificial ventricle, even though they be pulsatile, might harm the lungs and the systemic vascular bed. Fortunately, the elastic aorta will compensate for a great deal of abnormality in the aortic waveform (89). Nosé et al.

(94) found that if the air pressure driving a pneumatically-powered ventricle had a high, sharp initial peak, then the pulmonary arterial blood pressure attained a desirable wave-shape.

If sufficient venous return is to be obtained with artificial hearts, a proper circulating blood volume is necessary. Low blood volume also leads to poor arterial blood pressures. In many artificial heart trials by many groups, the blood volume had a tendency to decrease in the course of pumping, regardless of transfusion to replace the blood loss. In a series of experiments using an extracorporeal artificial heart, Atsumi et al. (9) found that 1) total vascular resistance decreased to about 70 percent of the initial level after one hour of circulation, 2) after three hours, the circulating blood volume had decreased to 67 to 75 percent of the initial value, and 3) blood pooling occurred mostly in the mesentery, intestine, and liver. Nosé et al. (92) found that both blood pH decreased and ascites formation occurred under conditions of low flow and poor venous return. They also stated that low molecular weight dextran was a useful infusion for increasing venous return, atrial pressures, and thus cardiac output.

Venous return is also aided by proper operation of the lungs. During normal inspiration the negative intrathoracic pressure tends to increase the venous return to the right heart. The increased volume of the lungs during

inspiration allows this increased flow to be accommodated with no increase in pulmonary artery pressure. On expiration the less negative intrathoracic pressure causes the venous return to the right heart to be reduced. However, there is a reduction in the volume of the lungs during expiration and the flow to the left atrium is augmented, causing the left ventricular output to increase. The phenomenon described above led Birtwell et al. (17) to state that the major contribution of the intrathoracic pressure was upon venous return to the right heart. This explains the less-than-optimum performance of an artificial ventricle under the adverse conditions imposed by an open-chest experiment.

There has been a variety of animals used in artificial heart experiments. Dogs have probably been the most popular species mainly because of their availability, cardiovascular anatomy, and ease of handling. One of the more serious complications in the dog has been the occurrence of thrombosis and emboli. It is possible that this complication is less of a problem in man, since it has been proved that man can live with heart valves of a type that will invariably lead to thromboembolic death in a dog (66).

For long-term trials, fewer complications have been reported by using other species. For total replacement of the natural heart with an artificial heart, the calf has been an effectual experimental animal (5). The use of the calf not only closely simulates human conditions (providing

that the calf's intra- and extracardiac fetal shunts are absent and that the bronchial artery blood flow is minimal) but also avoids the problem of blood clotting found in the dog (94).

Sheep have some distinct advantages over both dogs and calves. The heart in large sheep approaches the size of a human heart, the tidal volume of the lungs in sheep and man is very similar, and the thromboembolic phenomenon experienced with dogs is not as much of a problem with sheep (21). More important, the pulmonary shunting of blood that has been experienced in calves is not known to occur in mature sheep. Also, since the red blood cells of sheep are more fragile than those of man, dogs, or calves, sheep provide a more accurate index of the hemolytic potentials of the experimental procedures and devices (106).

When calves were used as the experimental animal for heart replacement, pulmonary hypertension and poor oxygenation frequently occurred as soon as the artificial heart began to pump blood (6, 117). The loss of oxygenation usually followed the development of an increased pulmonary arterial pressure. After prolonged extracorporeal circulation in dogs and to a lesser extent in man indication of similar impairment in pulmonary function is well known (5). Akutsu et al. (6) surmised several possible causes for this pulmonary damage. They went on to shown that a sudden large flow into the pulmonary circulation after there had been

occlusion for a certain period of time produced the insufficient oxygenation syndrome. They recommended a gradual transition from the pump-oxygenator to the artificial heart as dictated by the oxygenation saturation of the pulmonary venous blood. However, in a later set of calf experiments, the group reversed this recommendation and adopted a procedure in which the pump-oxygenator was stopped before the artificial heart started pumping (94). This abrupt change over did not affect pulmonary function. A sure reason for this event was not given.

Pulmonary complications may also develop if 1) pulmonary venous hypertension is allowed to occur during perfusion of the entire body (117) or 2) the output of the right artificial ventricle exceeds that of the left (94). This latter situation is analogous to left ventricular heart failure in the natural heart.

Experimental animals undergo quite a serious biologic shock in heart bypass and replacement trials. Thus criteria for survival need to be established. The indicators of the preservation of vital function might include femoral arterial pressure values, pupillary and deep tendon reflexes, recuperation of spontaneous respiration, and EEG findings (9, 79). Also for trouble-free pumping there must be minimum destruction of blood elements, no pulmonary edema, and no serious thrombi formation. The above criteria are by no means exhaustive but they include the more important

indicators of life. For a closed-chest heart replacement experiment, the really only acceptable test of success is the awakening of the animal even if for only a short period of time.

To conclude this section, a listing of the various causes of death in artificial heart experiments will be given. Disappearance of most of the reflexes and sustained detrimental values of the measured parameters are usually considered as signs of approaching death. The most frequent causes of death are as follows:

1. Pulmonary edema (9, 57, 121)
2. Clotting (9, 110, 121)
3. Bleeding in chest cavity (2, 79)
4. Pulmonary hemorrhage and cerebral damage (9)
5. Air emboli and hypovolemic shock (121)
6. Hepatic engorgement due to high venous pressure  
(57)
7. Metabolic acidosis (110)

The chart reproduced in Figure 11 is representative of the causes of death which have occurred with artificial hearts. It lists how various procedures can cause events to occur which ultimately result in the death of the experimental animal. Finally it should be obvious that many artificial heart experiments have been terminated due to mechanical breakdown of the artificial heart itself, the external machinery, or the monitoring system.

## Cardiac Work

A study of cardiac work is important both in heart replacement and heart assistance studies since it gives an idea of the expected energy demand to be placed on the artificial blood pump. For instance, it has been determined that a pump with an efficiency of 25 percent when supplied with 3.17 watts of mechanical power could circulate 3570 milliliters of blood per minute against a pressure of 100 millimeters of mercury (109).

Since the left ventricle expends the majority of the effort needed to propel blood through the cardiovascular system, most formulae for cardiac work are applied to the functioning of the left ventricle. The left ventricular work can be calculated from the formula (102)

$$W = PV + (1/2)(w/g) v^2$$

where W = cardiac work in kilogram-meters

P = mean aortic pressure in meters of blood

V = minute volume in liters

w = weight of blood in kilograms

g = acceleration due to gravity in meters per second<sup>2</sup>

v<sup>2</sup> = square of mean blood velocity in meters<sup>2</sup> per second<sup>2</sup>

The kinetic energy component represented by the second term of the formula is about five percent of the total work under



ordinary resting conditions (73). This latter term along with the work associated with the coronary blood flow is usually disregarded in the calculations.

In a practical sense, left ventricular minute work can be calculated as the product of left ventricular output in liters per minute divided by 100 and the mean systolic pressure in centimeters of water (76). Other formulae are evident in the literature but they differ mainly in the units used to measure the pressure (18, 73, 120). However, these formulae fail to show that the product of flow rate divided by 100 and the pressure does not lead directly to work in kilogram-meters per minute. For the above formula the conversion is

$$\frac{(1 \text{ liter}) (1 \text{ centimeter of water})}{(\text{minute}) (100)} = 10^{-4} \frac{\text{kilogram-meters}}{\text{minute}}$$

For a normal heart it has been found that the mechanical energy necessary to propel the blood of a resting human is about 0.25 gram-calories per minute (13). This is equivalent to 0.106 kilogram-meters per minute and includes the work of both ventricles.

Another practical way of determining cardiac work is by measuring the oxygen uptake of the cardiac muscle itself. This is closely associated with a parameter called the time-tension index (37). This index is the product of the pressure gradient against which the left ventricle must eject

blood into the aorta and the duration of that ejection. Sarnoff et al. (104) clarified that this index was the chief determinant of heart work, as measured by the oxygen consumption. One group applied the time-tension index to the design of their auxillary ventricle in an attempt to reduce left ventricular work (of the natural heart) by 40 to 50 percent (50).

### Power Systems

The overall success of an artificial heart is highly dependent on the type of energy conversion system which is selected to power such a mechanism. At the present time any artificial heart that is enclosed in the chest remains dependent on a permanent power supply from outside the body. Power transmission through the chest wall by means of wires (electrically) or tubings (liquid or gas under pulsating pressure) appears to be the most feasible method. Figure 12 demonstrates some of these possibilities.

The use of electricity is extremely inviting. Electrical energy is readily available, easily stored, and can be reliably controlled. In spite of these advantages, there are several problems inherent with the present electrical energy conversion systems which include excessive heat production, low efficiencies, and mechanical failure.

Three devices known for electromechanical means to drive an artificial heart are solenoids, electromotors,

and piezoelectric crystals.

The first artificial heart built by Kolff was driven by five small solenoids (65). An electromagnetic solenoid is an attractive prime mover for a prosthetic heart because it is simple and may be located outside the body as an air pump or incorporated in an artificial heart implanted in the chest.

There are three classes of solenoids that may be considered for energizing an artificial heart: d-c powered, a-c powered, and pulse powered (14). Kolff (64) discusses the fact that pulsing solenoids makes it possible to reduce their weight by 75 percent and yet have the same pumping capacity as d-c powered ones. Bindels (13) calculated values of efficiency of solenoids delivering the mechanical energy necessary to drive artificial hearts which were capable of supplying only basal flow rates and pressures. For a prohibitively large solenoid he found an efficiency figure of 98 percent.

Most motor-powered artificial hearts have been of two types. In one type, the motor, through a system of gears, pivots, and eccentrics, swings back and forth within a rigid housing (60). As it is driven back and forth, the body of the motor alternately compresses each ventricle against the housing and expels the ventricle's contents. In the second type of motorized artificial heart, the motor is fixed and a driven member performs the work (3, 100, 101).

The driven member can be a freely moving roller which alternately compresses either a set of ventricles or a single section of tubing. The other possibility for a driven member is a piston (24, 28, 62, 97, 99). Burns et al. (27) described a heart in which the built-in motor provided power (pressure head) to a hydraulic fluid which, in turn, was controlled by a built-in valve. The movement of the fluid caused the compression of the ventricles.

Various power requirements for motorized hearts pumping at physiologic flow rates and pressures have been reported. Low power levels of 15 watts and 10 watts have been attained, with the lowest reported value to be 7.5 watts (99, 100, 101).

The third mechanism utilizing electrical power is a piezoelectric artificial heart. A piezoelectric material changes shape on electrical stimulation and thus, in some respects, behaves as muscle tissue. The use of a material of this type permits a direct and efficient conversion of electrical energy to pumping energy. Loehr et al. (80) developed a piezoelectric device which pumped a working fluid of low density and viscosity back and forth to an artificial heart. Their crystals exhibited an excellent response to a variety of voltage excitation patterns. The units generated no heat and the conversion of electrical to mechanical energy was found to be nearly 100 percent.

The use of air eliminates problems of weight, size,

shape, heat production, and insufficient power, since air-driven hearts are smaller, lighter, more reliable, and easier to insert in the chest than artificial hearts that use motors or magnets (110). In this regard, the advantages of air-driven hearts are many. Air is a fairly efficient working fluid at the low pressures required and there is little energy loss from compression (45). Another advantage of an air-driven system is that more components of the system can be located outside the body, thus easing maintenance and repair. Operation of a pneumatic system with carbon dioxide provides added safety in case a leak should develop in a diaphragm of this type of heart since carbon dioxide dissolves in blood much faster than does air.

There are two types of air-driven power systems both of which require a tube into the chest cavity (73). In the "closed system" a rolling diaphragm pump, driven by a small motor, pumps air in alternate directions. There are other methods to produce the alternating air flow but the common factor to these systems is that the mass of working substance remains constant. The "closed system", if air is used, does not tend to produce excessive elevation in arterial pressure, since the systolic stroke is regulated by the actual arterial pressure.

In the "open system" power is derived from a compressed air line, oxygen tank, or a similar source. The systolic and diastolic times are regulated by electric or pneumatic

valves. This system works under high pressure and is so named because, during diastole the volume of air used during systole escapes from the pump. The "open system" requires constant regulation.

Hydraulic systems of the "closed" type have also been employed to drive artificial hearts (57, 80). Again a tube into the chest cavity is necessary.

It would be advantageous from the standpoint of avoiding infection to have no power connection (wires or air lines) through the chest wall. Kusserow (68) described a method in which a motor-driven permanent magnet on the outside of a tissue barrier drove a slave magnet within.

The most potentially attractive system for supplying energy to an artificial heart involves inductive coupling between a flat pancake-shaped coil on the surface of the chest and another similar coil within the chest. Schuder et al. (108, 109) demonstrated that such an arrangement could transport 50 watts through the chest wall with no apparent discomfort to the animal and without appreciable temperature rise in the coils or tissue. They further stated that this energy could be transported with losses in the coupling coils and tissue of approximately five percent of the transported power. The 50 watt figure given above is approximately 150 percent of the calculated power input to the biological heart of an adult under conditions of exercise (109). In seeking methods for improving the transport

efficiency, Schuder and Stephenson (107) also investigated the possibility of utilizing magnetic material, ferrites in particular, for the core of the receiving coil.

Biopsies from the tissues of dogs exposed on a chronic basis to an electromagnetic field equivalent to that required to transport 50 watts through the chest wall have been negative at two and three years (38). Furthermore, studies on heat dissipation in dogs have indicated that from one-fourth to one-half calorie per kilogram per second can be dissipated into the blood stream without ill effects (25).

Totally implantable nuclear power sources are also conceivable (26). If perfected, they would permit a complete and long-term replacement of a normal heart with no dependence on external energy sources.

The possibility of utilizing a relatively large skeletal muscle mass to power a small blood pump directly and continuously over extended periods of time has not been overlooked. Kusserow and Clapp (69) described such a method using the canine quadriceps femoris. They found that cellular injury took place under the conditions of the experiment, despite the satisfactory kinetic performance of the muscle throughout the period of stimulation. Another disadvantage of this method is that it necessitates wires passing through the chest wall to stimulate the muscle mass.

## Control Systems

The objectives of most research groups concerned with artificial heart development encompass three design problems: 1) the artificial heart itself; 2) an efficient and suitable power source; and 3) a system for the control of the output of the artificial heart in response to changing needs of the experimental subject. Artificial ventricle systems have been designed which reasonably duplicate the flow and pressure waveforms of the natural intact heart (89, 111). However, the development of an automatic control mechanism for these artificial pumps is a different and more difficult type of design problem.

The normal heart is controlled through nervous and humoral channels which are responsive to many body functions and actions. When an artificial heart replaces the normal functioning heart, the problem of control becomes exceedingly important. Almost any air-driven artificial heart of the diaphragm type that does not have a fixed stroke volume will, on its own, follow Starling's law to some extent (114). (The consequence of this law is that the amount of blood pumped is proportional to the degree of diastolic filling). For adequate performance, however, more sophisticated control is absolutely necessary. The control system must be concerned with the transduction of appropriate physiologic signals, processing these signals and



making decisions based upon them, and finally actuating the artificial device. These actions should be done with minimum demand upon voluntary controls and artificial energy sources.

It has been said that "it is a combination of complexity and ignorance (or uncertainty) that forces one to employ feedback control" (11). If the operating characteristics of the circulatory system were fully understood, the system's responses to exercise, drugs, and stimuli would be known. Then on the basis of this knowledge the behavior of the system could be predicted well in advance and the proper action to take to hold a control parameter in line with a desired level could be computed.

Unfortunately the literature describing the automatic control of artificial hearts is not abundant. The reason for this may be that the duplication of the primary function of the normal heart (to pump blood) was envisioned to be a much easier task than the duplication of the complex and accurate regulation of its action.

The first control systems, and many now in trial use, depended on an easily obtained method of control -- human attendants. By observing several physiologic parameters, a human operator (or sometimes an entire team) could easily adjust the operating point of an artificial heart. This means of control, however, is a waste of both money and human talent.

The main function of the heart is to provide an adequate cardiac output. Since cardiac output is the product of heart rate (in beats per minute) and stroke volume (in liters per beat), there are two means of effecting control of heart output. With air-driven artificial hearts changing the stroke volume seems to be the most popular method. With motor-driven artificial hearts changing the cycle rate predominates.

The Cleveland Clinic group has published two articles describing design criteria for artificial heart control systems (58, 89). Nosé (89) stated that for optimum performance, the control of right and left artificial ventricles should be separate and independent. This criterion is not universally accepted. In any event the control system must at all times provide sufficient blood flow to avoid tissue ischemia. The blood flow rates of each ventricle should be balanced. However, it is not necessary to have this equality hold on a beat-to-beat basis. It is probably adequate to base the flow equality on a few minutes timing (94). Maintenance of flow balance avoids pooling of blood both in the pulmonary circuit and in the systemic circuit and prevents air emboli and the disruption of pump-to-vessel connections. The use of atrial blood pressure as a control parameter provides some degree of flow balance. This will be described later.

There have been several notable means of external

control developed to regulate an artificial heart. However, the greatest effort has been expended in designing self-regulating artificial hearts, since self-regulation constitutes a very desirable means of control.

The role that atrial pressure has in the regulation of the normal heart was described earlier (Starling's law). Not all development groups considered this law to be of much importance in their control systems. However, the majority of the artificial heart developers did at least recognize the necessity of atrial pressure regulation and many utilized it in their control systems. Nosé (89) stated that the feedback system that controlled the artificial device should be sensitive to the venous pressure and that this input pressure should be kept within a desired range. He further stated that this mechanism itself was sufficient. Venous pressure regulation of an artificial ventricle's fluid output prevents both abnormally high and low venous pressures from occurring and thus inhibits the venous system from experiencing overdistension and collapse.

The efficacy of atrial pressure regulation is probably best summed up by Dr. Jesse Meredith (82) when he commented on the work done by Pierce et al. (97): "If one assumes that under standard conditions the heart is a constant flow pump or a constant current generator and that it is controlled by pressure to produce a constant flow under a given set of standard conditions, also if one considers that under normal

conditions the venous return is a good measure of the blood flow, and if one agrees that central venous pressures are proportionate to venous return, then the device described by Pierce is a device which tends by negative feedback to produce a constant cardiac output. By this concept it has an important virtue in development of replacements for the heart."

An added benefit of having ventricular output controlled by atrial pressure is that it automatically leads to an adjustment of the amount of blood pumped by each side of the heart (66). Flow equality occurs since a deficiency on one side inevitably leads to an increase in venous pressure on that side which, in turn, increases the cardiac output on that side.

Norton, Akutsu, and Kolff (88), Atsumi et al. (9), Hastings et al. (56, 57), and Burns et al. (26) have based the construction of their hearts and control systems upon the hypothesis that cardiac output should be controlled by venous or atrial pressure. Nosé et al. (94) controlled their air-driven pumps by changing the air pressure to the individual ventricles. They attempted to maintain right and left atrial pressures within a range of 10.0 to 15.0 centimeters of water (7.36 to 11.03 mm. Hg). Kolff et al. (66) found that, by using a N.A.S.A. servomechanism, there was an instantaneous response in change of output from one side of the circulation to the other. They stated that this

action was the strongest argument they knew of to predict the success of a regulating mechanism in which the atrial pressure determined the cardiac output of the ventricle.

Seidel et al. (110) developed an artificial ventricle which permitted an increased diastolic filling and hence an increased stroke volume proportional to a rising venous pressure. They regulated the driving air pressure so that the blood chamber just emptied within a given systolic time. As long as the chamber completely emptied during systole, the artificial ventricle used venous pressure for the automatic adjustment of its output.

Pierce et al. (97, 98) and Burney et al. (24) have designed a control system based on continuous regulation of venous pressure. Their system used two integral diaphragm pumps of the piston type which were driven by small d-c motors. Thus each pump required only a source of electrical power. The motor speed and hence the pump's fluid output changed as a function of the integral of the venous inflow pressure. A problem with this system was that rapid and undesirable fluctuations in pump speed were caused by pressure transients in the inflow line. Mechanical damping of the pressure catheter eliminated this.

The control system described in this dissertation follows the above idea except that continuous correction is not provided. Also the system is designed to regulate a pulsating pneumatically-powered artificial ventricle.

Recently Nosé et al. (90) described a very sophisticated control system which duplicated the Starling regulation of the normal heart. They found that the normal right ventricular curve (fluid output versus filling pressure) had a slope of 4.3 liters per minute per millimeter of mercury at the operating point. Using a closed-loop computerized control system they were able to duplicate this sensitivity in vivo with an artificial heart. The command signal to the pressure servomechanism was modulated by the average atrial pressure in such a way that an increase in atrial pressure proportionally increased the strength of contraction of the artificial heart.

Edwards and Bosher (40) described an automatic control system based on both arterial and venous pressure regulation. Their argument was that these pressures are the only variables which instantaneously reflect changes in blood flow and thus they should govern the arterial delivery rate. (Their argument is possibly true since some measurable indices of body chemistry change only after the blood has passed through the patient's tissues for metabolic exchange). Their system exhibited a seven to eight second lag between the time a correction was made and the time when the change was noticed in the circulatory system. The delay in feedback caused the system to oscillate. Oscillation is also a problem with other control systems (35, 41, 97). Incidentally the Edwards and Bosher control system was capable

of changing the cardiac output at a maximum rate of two liters per minute per second.

A major obstacle in automatic control is that of inadequate blood return from the animal's circulation to the artificial ventricle. Liotta et al. (79) concentrated their efforts on regulating the end-diastolic volume of their artificial heart so as to 1) maintain a systolic residue of one-third of the stroke volume to avoid excess trauma to the blood, 2) maintain filling pressures of 10.0 to 15.0 centimeters of water without provoking negative pressure in the atria, and 3) provide maximum filling time.

Since the natural heart serves as a recipient of many signals from the body it is obviously an important element in normal control. If the pacemaker of the natural heart were to be left intact and functional, it could be utilized to pace an artificial heart (54). This would allow for at least partial biologic control of cardiac output. This method of biologic control has been utilized but not without some problems. Liotta et al. (78) found that attaining an acceptable degree of reliability was a dilemma. Motion artifacts and noise were problems. However, the placement of electrodes appeared to be relatively unimportant and ventricular fibrillation never occurred.

Many of the artificial hearts developed had a high degree of intrinsic control and needed no sophisticated external control system. An intrinsically-controlled

ventricle must obey Starling's law as closely as possible. To do this, provision must be made to 1) allow the ventricular volume to vary and 2) limit ventricular pressure during diastole. These requirements eliminate rigid mechanically-coupled driving units and mechanically-powered hydraulic units. However, pneumatic units easily meet these requirements and also allow for easy incorporation of other desirable characteristics. Akers et al. (1) developed a system based on the above criteria for a self-regulating device which contained both a specialized air pulse generator and a bypass pump.

The fluid amplifier, a device for controlling the flow of fluids without moving parts, seems to be an appropriate intrinsic control mechanism for an artificial heart. Several fluid amplifier-controlled artificial hearts have been built which demonstrated relatively stable control of atrial pressure (10, 33, 121).

The operating principles of fluid amplifiers are excellently described in an article by Angrist (7). The advantages of an artificial heart controlled by a fluid amplifier are listed in Figure 13. It should be obvious that the fluid amplifier provides control flexibility not enjoyed by pneumatic control elements.

Barila et al. (10) developed a plastic ventricle which was powered by compressed air and controlled by a fluid amplification system. The flow rate of the ventricle was



governed by the filling blood pressure, the resistance of the outflow tract, and the driving air pressure. The air pressure applied to the ventricle was regulated so that the minimal force necessary to just overcome the outflow resistance was used. The pump responded automatically by an appropriate alteration of both stroke volume and pulse rate. The pump produced flow rates from 0.5 to 10.0 liters per minute at rates of 20 to 125 pulses per minute. When tested in vitro, the pump produced very little hemolysis.

Castañeda et al. (33) developed the Army Artificial Heart, a fluid amplifier-controlled pump, whose operation was governed by four factors: 1) systolic air pressure; 2) pulse duration; 3) pulse rate; and 4) ventricular suction. The fluid output varied directly with changes in filling pressure and inversely with output resistance. They also found that all the factors except systolic air pressure played relatively minor roles in determining the fluid output.

Woodward et al. (121) designed an intrathoracic fluid amplifier-controlled artificial heart which maintained venous pressure properly when adequate venous return was present. Their intrinsic control system allowed the ventricle to fill more rapidly when the venous pressure was high, and this increased the pulse rate. Conversely, low venous pressure caused the ventricle to fill more slowly and the pulse rate decreased. They also stated that high

venous pressures resulted in somewhat larger stroke volumes, but that pulse rate was the dominant means of flow regulation.

Although it is thought by some that automatic control of an artificial heart is a relatively simple problem, no one can say that it is a minor field of investigation. With implant trials of long duration a very definite possibility it may very well be that additional serious post-implant problems will be observed in vascular tone, blood clotting, healing, and the matching of subject and machine control systems. These complications may be due to very subtle incongruities in the performance of the mechanical system with respect to the optimal performance of various body systems. Optimizing the response of the physical control system to those controls operating in the living subject will tend to minimize or eliminate any occurrence of irreversible circulatory embarrassment. The development of a miniaturized, implantable, self-regulating control system responsive to the body's own remaining signals is a fascinating challenge to both medicine and engineering.

#### Cardiac Assistor Devices

There is another area of prosthesis development which can be tied in with artificial hearts. This area is concerned with mechanical devices to assist, not replace, the failing heart. Some research groups would rather leave the diseased heart intact and replace or supplement only the

heart's function, thus enabling the heart to heal. These circulatory assistor devices must 1) reduce the ventricular diastolic pressure of the failing heart chamber or reduce the flow of the weakened ventricle, 2) provide sufficient blood flow to the body, and 3) not cause further damage to the heart or other vital structures.

Methods of accomplishing prolonged heart assistance include: 1) counterpulsation or arterio-arterial pumping; 2) diastolic augmentation; 3) left ventricular bypass; 4) synchronous respiration; and 5) automatic heart massage.

No matter what method of assistance is used, it has been found that to relieve the load of the left ventricle the pump circuit has to carry at least 50% of the cardiac output (36). Also it is difficult to carry out controlled evaluations of the efficiency of assistive techniques since the experimental animal cannot readily be placed into a standardized degree of cardiac failure for testing the beneficial effects of mechanical cardiac assistance.

Counterpulsation aims at increasing coronary arterial perfusion by raising the pressure during diastole and decreasing the work load of the left ventricle by lowering the pressure during systole (18). The method is based on the concept that a competent aortic valve effectively isolates the left ventricle from the increased diastolic perfusion pressure created by a synchronous pulsatile pump. Most of the machines have been designed to withdraw blood

from the arterial tree during systole with consequent reduction in systemic resistance and to return it during diastole, using a portion of the electrocardiogram as a triggering signal. Callaghan et al. (30) found that if myocardial work was to be lowered, not only must the systolic arterial pressure be reduced, but the end-diastolic pressure, which represents the static load on the heart, must also be reduced. Mantini et al. (81) found that synchronized counterpulsation was a useful therapeutic remedy in experimental canine cardiogenic shock.

There are several ways of accomplishing counterpulsation. Callaghan et al. (30) described a computer-automated counterpulsation system which was connected to a femoral artery. A cardiac homotransplant with an insufficient aortic valve can be synchronized to function as an arterial counterpulsator. Gannon et al. (46) demonstrated this novel method by suturing a donor heart to various portions of the thoracic or abdominal aorta in dogs. They obtained favorable results with a maximum survival time of 14 days.

Diastolic augmentation of pressure in the aorta, like counterpulsation, promotes coronary flow with no additional burden on the left ventricle. Diastolic augmentation differs from counterpulsation in that during heart systole the augmentor device remains passive and becomes active only during heart diastole.

Intrathoracic methods of diastolic augmentation will be discussed first. Only one biologic method has been attempted -- the use of a skeletal muscle to assist myocardial function. Kantrowitz (61) wrapped the autogenous left hemidiaphragm around the distal thoracic aorta and applied intermittent stimulation to cause muscle contraction in time with normal heart diastole. Liotta et al. (76) also applied diastolic compression to the descending thoracic aorta, but used a five to eight centimeter length of pneumatic sleeving. Moulopoulos et al. (87) developed an augmenting system which periodically inflated and deflated a long, narrow balloon inserted in the descending aorta. The balloon was inflated during diastole of the natural heart's cycle and increased the diastolic blood flow to the periphery.

Nosé et al. (93) developed what they named an auxiliary ventricle. This pneumatically-operated, rubberized, collapsible bulb was implanted end-to-side in the ascending and descending aorta, thus bypassing the aortic arch. The valveless unit filled passively during normal heart systole and then during diastole it expelled its blood back into the aorta. In later papers in which the same pump was used, the ascending aorta was ligated above the unit to increase blood flow in the auxiliary ventricle and thus diminish the risk of clotting (50, 91). Birtwell et al. (16) developed an externally actuated, subcutaneous "in-series" prosthetic

left ventricle. The ventricle was energized by applying an external pneumatic actuator to the device. Infection problems were reduced considerably since the skin barrier was intact.

The most notable method of extrathoracic diastolic augmentation is that of external compression of the lower extremities. External compression is an effective approach for assisting the circulation for long periods since the requirements of cannulation, anticoagulants, and anesthesia are eliminated. Dennis et al. (37) found that, in the dog, the arterial blood expressible was of the order of magnitude of three milliliters per kilogram of body weight. In a study by Birtwell et al. (15) the data indicated that venous return and aortic pressures could be modified effectively so as to reduce left ventricular work and, at the same time, increase cardiac output.

The "in-series" auxiliary ventricles mentioned above aid the heart by reducing the pressure work of the heart. This is in contrast to ventricular bypass devices (or "shunt" auxiliary ventricles) which aid the heart by reducing the flow work of the heart. Much effort has been concentrated on left ventricular bypass devices and procedures due to the relatively higher occurrence of left ventricular failure over that of right ventricular failure.

The air-driven, tube-type pump developed by Liotta et al. (73) performed successfully in 47 left ventricular

bypass procedures in dogs. The pump functioned up to 44 hours in one case. This group's pump and their later ones (76, 77, 78) were in the form of small U-shaped tubes and were connected between the left atrium and the descending aorta. Birtwell et al. (16) developed a similar pneumatically-powered device for use as a left ventricular shunt. Akers et al. (1) and Hall et al. (53) described a paracorporeal bypass pump powered by air pressure. The bulk of this pump was on the outside of the body. Two tubes led into the chest cavity for connection to the left atrium and to the aorta. The use of two artificial ventricles in a double ventricular bypass procedure has also been reported (75).

Roughly in the same area of ventricular bypass devices was an intraventricular artificial heart described by Hall et al. (54, 55). They developed silicone rubber pumps which were placed inside the contours of the right and left ventricles. The sac-type pumps incorporated atrioventricular valves and utilized the existing aortic and pulmonary valves.

Right heart assistance by synchronous respiration is based on the hypothesis that the lungs can be made to exert an optimal pumping effect if the size of the pulmonary vascular bed can be increased at low alveolar pressures during right heart systole, and decreased by a higher alveolar pressure during diastole (113). Naturally this type of assistance has a large influence on the pulmonary circulation.

Birtwell et al. (17) found that the venous return to the right heart responded quickly to synchronous changes in intrathoracic pressure. Soroff et al. (113) studied the effect of synchronizing the inflation and deflation of the lungs with different portions of the cardiac cycle. They found that, with proper phasing, the pressure which must be exerted by the right ventricle was diminished.

The last method of cardiac assistance to be discussed is that concerned with heart massagers. In this method, the cardiovascular system remains intact. This eliminates both a very large operative procedure and total body heparinization for prolonged periods. Also the normal endocardium, as well as the normal cardiac valves, are functionally retained. The heart muscle exerts force by contracting and shortening, both of which are simulated by the massage devices. A final advantage of this type of cardiac support is that it can be used with either a fibrillating or a failing heart.

Zajtchuk et al. (124) developed a heart-shaped plastic enclosure into which the heart was slipped. Pulsating air pressure provided the energy to massage the heart. Upon histological examination of the heart, liver, lungs, kidney, and blood elements no tissue damage could be demonstrated at the time of sacrifice of the experimental animals.

Anstadt et al. (8) described a pneumatic instrument which assisted the heart during both the systolic and



diastolic phases of the cardiac cycle. The force was applied exclusively to the walls of the ventricles with no inappropriate force applied to the atria. They obtained cardiac outputs from 70 to 100 percent of control values in dogs during ventricular fibrillation and had survivals often up to eight hours of total circulatory support.

Both of the previously mentioned massagers caused the assisted heart to go into systole with the application of air pressure. The rubber massager developed by Kolobow and Bowman (67) normally compressed the heart into its systolic form. Upon the application of suction, the device allowed the heart to go into its diastolic form. This device functionally simulated the contracting atria in addition to energizing both ventricles.

## THE ARTIFICIAL VENTRICLE SYSTEM

## The Artificial Ventricles

Three pneumatically-powered artificial ventricles were developed in the course of this study. All of the models were oversized prototypes designed mainly for the evaluation of the power and control system during extracorporeal use. None of the models were designed for intrathoracic implantation. Also, the artificial ventricles were used only in short-term trials during which the natural heart of an experimental animal was bypassed but left in place. All of the ventricles (except Model I) operated in a position adjacent to and outside of the chest. Connections were made to the animals' great vessels by short polyvinyl chloride catheters.

The design, fabrication, and testing of only artificial ventricles were originally undertaken. The hope was to utilize the intact atria of a deventricularized heart to serve as filling and pressure-buffer chambers for the artificial ventricles. However, since none of the ventricles were implanted within the chest and only heart-bypass experiments were conducted, the fabrication of artificial atria was necessary. These small, collapsible chambers not only facilitated ventricular filling but also absorbed the negative pressure impulses which occurred during the filling phase and which tended to collapse both the artificial

atria and the great veins.

The basic construction and the operating principle of all three models are essentially identical and all are powered by short pulses of compressed air. All models employ small flap valves to insure unidirectional liquid flow and a thin stretchable diaphragm to transfer the pneumatic energy into liquid pumping energy. The liquid stroke volume is altered by changing the pressure of the air being pulsed to the ventricle. This is the means by which the automatic control system functions to regulate the ventricle's liquid output.

The flap valves used in all three artificial ventricles are cut from thin (0.050 inch) medical-grade silicone rubber sheeting. The valves for the Model II ventricle are shown in Figure 14. There are two pieces to each valve unit -- the flexing flap part (C) and the stationary seating part (D). The seating part is not necessary if a proper valve seat is constructed into each valve housing. However, the use of a seating part of like material does compensate for roughness and unevenness in the machined valve housings and provides an excellent seal to any backflow of liquid.

The operation of the flap valves is electrically analogous to the action of a diode. The valves operate entirely passively and offer little resistance to forward liquid flow while offering considerable resistance to reverse liquid flow.

These valves would not be considered adequate for long-term use since there is a substantial amount of flexing along the hinge line. Also with repeated use, the flap part of the valve has shown some tendency to take on a permanent "set" in a partially opened position, thus requiring greater backflow of liquid to close the valve. Redesign of the valve or the substitution of a better material would help to solve this problem. Ease of construction and maintenance and small displacement volume were distinct advantages of these valves. The flap valves were used throughout the project since appreciably better valves of other types were neither readily available nor adaptable.

As was mentioned previously, all three artificial ventricles follow the same principle of operation. The method of operation will be described with reference to Figure 15 which is a cross-section view of the Model II artificial ventricle. A flexible diaphragm divides the ventricle into two compartments, a liquid chamber and an air chamber. When a volume of compressed air is pulsed into the air chamber, the diaphragm bulges upward into the blood chamber (emptying phase). This action closes the inlet flap valve and displaces a volume of liquid through the flap valve in the outlet port. During the filling phase the compressed air is vented to the surrounding atmosphere, thus allowing the diaphragm to recoil to a rest position (or beyond). This action creates pressure gradients which close the outlet valve and open the inlet

valve, thus allowing the liquid chamber to be refilled through the inlet port. (The amount of refilling is a function of the input filling pressure, the inlet port diameter, the liquid volume available for filling, the elasticity and degree of stretch of the diaphragm, and the time allowed for the filling phase.) The ventricle is now ready for the next pulse of compressed air and the cycle repeats itself. A continued series of air pulses, then, causes a periodic liquid pumping action to take place.

The three artificial ventricles are shown in Figure 16. Model I was used only to ascertain the feasibility of the pumping method. It was not used in any animal experiments. The size, weight, and volumes of interest pertaining to this ventricle can be found in Table 1. Design specifications were made to conform to data of the functional performance of the left ventricle of a 20 kilogram dog.

The body of the Model I ventricle was made of plexiglass. The two chambers of the pump were held together with a ring of eight screws. The flexible diaphragm separating the air and blood chambers was cut from a section of thin (0.030 inch) rubber drainage tubing. Connection to the air chamber was made by attaching an air hose to a brass adapter which was sealed into the air chamber. Two short lengths of polyvinyl chloride tubing (1/2 inch I.D. x 11/16 inch O.D.) made up the inlet and outlet fluid lines. The tubes were bonded to the plexiglass valve housing with a silicone

rubber medical adhesive.<sup>1</sup> The silicone rubber flap valves were attached inside the valve housing in a similar fashion.

The purpose of the large adjustable air chamber in the Model I ventricle was to determine the optimum size for an air chamber. A large chamber tends to damp any fast pressure rise introduced into the chamber. This absorption of pneumatic energy, then, lowers the peak pressure seen in the blood chamber and lengthens the rise time of the pressure pulse. The use of too small an air chamber can result in very rapid and detrimental pressure changes in the fluid output line. It was found, however, that an external air chamber in series with the air line functioned as an adequate damping mechanism. Thus as small an air chamber as possible was chosen for all subsequent models. This choice was obviously advantageous from the standpoint of possible later intrathoracic implantation.

Following completion of tests on the Model I ventricle, a second prototype artificial ventricle was designed (Model II) and two units were constructed. These pumps were used extensively, in in vitro tests and exclusively in both in vitro and in vivo control studies. These ventricles were made of medical-grade silicone rubber and teflon.

Medical-grade silicone rubber materials presently offer

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<sup>1</sup>Silastic R (Type A), Dow Corning Corporation, Medical Products Division, Midland, Michigan.

distinct advantages over other synthetic materials for use in artificial ventricles (22). They possess a low degree of biological reactivity. They are flexible and can be molded into practically any desired shape. A disadvantage is that they are somewhat friable. Also since they are good electrical insulators, it appears that the inability to dissipate surface electric charge might actuate the clotting mechanisms of normal blood (22). Advances in materials research, either in improved silicones or other new products, will most likely eliminate the disadvantages listed above.

Teflon similarly possesses low reactivity in the internal environment of the animal body. Teflon construction has presented two major difficulties. Though it can be machined to a desired configuration, it is difficult to produce fluid-proof threaded connections. Secondly, its low degree of chemical reactivity makes it very difficult to bond teflon to itself or to other materials with adhesives or encapsulating materials. However, more reactive synthetic materials, when made blood-compatible by coating with heparin, offer distinct advantages in the design of blood-handling devices (49, 119).

All of the parameters of the Model II ventricle except overall dimensions were designed to approximate the cardiovascular parameters of a 20 kilogram dog. The parameters pertaining to this ventricle can be found in Table 1. Each one-ventricle unit has been used in short-term right- and

left-ventricular bypass experiments to assess servomechanism control of "cardiac" output. The teflon unit has also been operated singly to evaluate other components in the entire system. In addition, a single unit has been found to perform as well as, if not better than, a commercial blood pump for extracorporeal circulation during total heart-lung bypass procedures.

The disassembled teflon ventricle is seen in Figure 17 and is shown diagrammatically in Figure 15. The identifying letters in the two figures correspond. The ventricle is basically a two-chambered cylinder (A). Two valve housings (B) each of which contains a one-way flap valve (C, D) are threaded into a cover (E). The cover is threaded into the cylinder. The depth to which the cover is inserted determines the volume of the artificial ventricle's liquid chamber. The cover is then usually sealed with a silicone rubber adhesive. The other section of the main cylinder is the air chamber. The thin (0.010 inch) diaphragm (F) is attached (with rubber cement) to a thin plexiglass ring (G). This member and another thin plexiglass retaining ring (H) are seated onto a ledge of the main cylinder and secured with a teflon threaded ring (I). Finally another cover (J) with its air hose connector (K) is threaded into the main cylinder. Note that the volume of the ventricle's air chamber is also variable. The simplified construction of this ventricle made its maintenance and cleaning a simple task.



Figure 17 also shows the accessory artificial atrial chamber (L) which is connected to the ventricle's fluid input port. This chamber buffers the pressure transients developed by the elastic recoil of the diaphragm during the filling phase. It is made of 0.020 inch dacron-reinforced silicone rubber. This chamber greatly aided the ventricular filling and therefore the pump's liquid output. Other artificial ventricle designers have reported the need for similar accessory chambers (92, 94, 121).

Again, this teflon model was not designed for intrathoracic implantation. It was always operated in a position outside the chest and was connected to the great vessels by short, flexible plastic catheters (3/8 inch I.D. x 9/16 inch O.D.). The ventricle proved to be quite acceptable for the experimental trials in which the intrathoracic placement of a pumping device was not required.

Due to the small size of the liquid orifices in the Model II ventricle, abnormally high blood pressures occurred with attempts to obtain adequate blood flow rates in larger dogs. Thus a third extracorporeal model was fabricated. This model was designed not only with larger orifices but also to exhibit minimal stretching of the diaphragm at proper stroke volumes. No in vivo control studies were conducted with this model and only a few in vitro pumping tests were done on it.

The main body, valve housings, thin rings, and covers

of the Model III ventricle were made of plexiglass. See Figure 16. Medical-grade silicone rubber, again, was used both for the one-way flap valves and the stretchable diaphragm. This was the only ventricle to be explicitly designed for a long pumping life. It has been suggested that if the amount of stretch in a piece of silicone rubber is less than ten percent of its original length, the dynamic life of the piece is greatly increased.<sup>1</sup> This ventricle, then, was designed to have a liquid stroke volume of 0 to 100 milliliters with a corresponding linear stretch in the diaphragm of no more than ten percent. The parameters pertaining to the Model III ventricle can be found in Table 1.

Although this artificial ventricle was designed as a substitute for the natural ventricle of a large dog (weight greater than 20 kilograms), it also found limited use in several heart-bypass experiments on sheep. In these experiments the ventricle was quite inadequate due to 1) too thin a diaphragm (0.005 inch) and 2) improper extracorporeal placement of the device. Negative pressures resulting from large vein collapse caused the thin diaphragm to be pulled to the top of the liquid chamber thus severely affecting the filling process. Improved ventricular placement and a

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<sup>1</sup>Cholvin, Neal R., Professor and Chairman, Biomedical Engineering Program, Iowa State University, Ames, Iowa. Seminar by Mr. Silas R. Braley, Director, Dow Corning Center for Aid to Medical Research, Midland, Michigan. Private communication. 1967.

thicker diaphragm would have helped but sheep trials were abandoned and no further tests were conducted on the Model III ventricle.

One member (Cholvin) of the Iowa State University artificial heart group has designed an implantable two-ventricle model which conforms to the shape of the natural heart. This model replaces only the animal's ventricles -- the natural atria remain intact and are used for attachment and flow-buffering purposes.

The performance of the artificial ventricle as a source of pressure and flow is dependent on many variables: 1) pulse rate; 2) percent systolic time (duty cycle); 3) pulsed air pressure; 4) positions of the air-bleeder valves; 5) output pressure head (load); and 6) input filling pressure. A family of curves showing how liquid output varies as a function of any of these variables could be drawn. However, probably the best way to depict the operation of the artificial ventricle is to show how liquid output varies with 1) the output pressure head and 2) the input filling pressure. Varying the pulsed air pressure in each test set-up, then, will generate a family of curves. The remaining variables must be kept constant.

Following the ideas just described, liquid output tests were conducted on the Model II artificial ventricle. In each experiment water was used for the circulated fluid. The pressure conversion factor used was: 1.0 millimeter of

mercury (mm. Hg) = 1.36 centimeters of water. The other constants common to both tests were: duty cycle -- 33 1/3 percent; rate -- 70 beats per minute; and air-bleeder valves -- closed. The same ventricle was used in each case. The results of these experiments are depicted in Figures 18 and 19. It should be mentioned that these figures merely demonstrate the in vitro capacity of the pump and lack the utility of in vivo studies.

Figure 18 clearly shows that, with constant input filling pressure, flow rate and output pressure head are inversely related at any given level of pulsed air pressure. Thus the ventricle is load sensitive. This is to be expected since the ventricle is not a fixed displacement pump. The maximum flow attained in this test was 2.6 liters per minute. Slightly higher flow rates are possible but the rubber diaphragm is prone to break if greatly overstressed. It should be mentioned that the output pressure head is analogous to the diastolic pressure level in the intact human circulatory system.

The model II ventricle failed to demonstrate any reliable degree of intrinsic regulation. That the fluid output was not a function of input filling pressure indicated that the ventricle did not follow Starling's law. This property is demonstrated in Figure 19 where the output pressure head was held constant while the input filling pressure was varied. The pulsed air pressure was also varied to obtain a family

of curves. The majority of the curves show relatively little variation in flow rate as the input filling pressure was varied from -10.0 to +15.0 mm. Hg. These results were unexpected since most diaphragm-type pumps that do not have a fixed stroke volume show some degree of self-regulation. Other artificial ventricles have been built which do show some intrinsic control by means of input filling pressure (3, 5, 56, 57, 60, 100).

The lack of self-regulation was probably caused by 1) an unlimited filling volume available and 2) the rubber diaphragm being maximally stretched during each systole (for a given level of pulsed air pressure). During diastole the diaphragm recoiled to its rest position and created enough negative pressure to fill the liquid chamber to the same level each time. The Model II ventricle may be self-regulating when used in vivo, however, since 1) venous return volume is not unlimited and 2) during diastole the recoiling diaphragm often creates enough negative pressure to collapse the great veins, thus further limiting venous return.

A distinction should be made between the distensible diaphragm ventricle (the type used in this study) and the rolling diaphragm ventricle. The latter type of diaphragm, being relatively inelastic, requires the application of a negative air pressure during the filling phase to assist in moving the diaphragm back to its pre-systolic position. The degree of diastolic filling, then, is dependent on both the

liquid input pressure and the level of negative air pressure applied (other factors being constant). Thus, if the level of negative air pressure was not too great (to cause venous collapse), a rolling diaphragm artificial ventricle would be expected to exhibit a dependency of stroke volume on the liquid input pressure. A rolling diaphragm ventricle which does show this dependency has been reported (88).

A single hemolysis study was conducted on one of the Model II artificial ventricles using freshly drawn and heparinized canine blood. The degree of hemolysis, as measured by the amount of free plasma hemoglobin present in milligrams per 100 milliliters of whole blood, can be plotted as a function of time, the amount of blood pumped, or the number of passages of blood through the test circuit. Since these three variables are interrelated (see page 50), time was used as the independent variable.

A graph of plasma hemoglobin determinations made at specific times over a continuous 75 minute period is shown in Figure 20. The ventricle pumped into a constant pressure head of 80 mm. Hg. The remaining pump adjustments were also held constant: rate -- 70 beats per minute; duty cycle --  $33 \frac{1}{3}$  percent; input filling pressure -- 5.0 mm. Hg; and air bleed-off valves -- closed. The initial priming volume was 800 milliliters and the blood flow rate was adjusted to two liters per minute. The graph shows that the destruction of red blood cells increased approximately linearly with

time, a phenomenon previously reported (118).

The index of hemolysis (I.H.), as determined by the method of Wesolowski (118), was 0.1533 grams of hemoglobin released per 100 liters of whole blood pumped for the first 30 minutes, 0.217 for the second 30 minutes, and 0.1748 for the overall 75 minute period. These values compare favorably with reported index of hemolysis ranges of 0.17 to 0.29 with canine blood (31, 101). Obviously, the silicone rubber flap valves caused some of the red blood cell destruction. Additional damage could have resulted from 1) a high blood flow velocity through the ventricle's output port, 2) incompatibility of blood with the components of the test circuit, and 3) blood turbulence both in the return line and in the filling reservoir.

#### The Pneumatic Power System

An important aspect of artificial heart research is that of power transmission and conversion. Several sources of power are potentially useful for developing in an artificial device the power necessary to circulate blood. Among these are electric motors, hydraulic and pneumatic pumps, and nuclear devices. Other possible power systems include electromechanical converters utilizing electrical power transfer through inductive coupling (107) and conversion of biological mechanical energy utilizing the piezoelectric effect (80). In both of these latter instances there need be no

direct connections between the thoracic cavity and external body surfaces.

Many research groups concerned with the problem of power have selected compressed gases to drive their artificial ventricles. Pneumatic methods are characterized by high transmission efficiency, relatively great energy storage capacity, easy controllability, availability, and portability (19). However, the type of power unit to be used is specified, to a large extent, by the desired operating characteristics of the ventricle.

The artificial ventricles used in this study were powered by compressed air in an "open system" arrangement. The pneumatic power system was designed to be reliable and to adequately match the power requirements of all artificial ventricles developed in this study. It has proven itself to be sufficiently capable to perform these tasks. Basically the power system simply controls the movement of compressed air to and from the artificial ventricles. Oscillator-driven electromagnetic solenoid valves function to control the rate and duration of the pulses of compressed air. The amount of air pulsed to a ventricle in each cycle is a function of 1) the pressure of the air source, 2) the amount of time the solenoid valve is open, 3) the degree of air bleed-off in parallel with the ventricle, and 4) the load imposed upon the ventricle by the animal's circulatory system.

A block diagram of the pneumatic power system for one



ventricle is shown in Figure 21. External to the actual power module are the source of compressed air, an "on-off" air valve, and the artificial ventricle. The pressure of the air entering the module (approximately 90 pounds per square inch) is indicated on a 0-100 pounds per square inch pressure gauge (labeled LINE PRESSURE). At the point where this gauge is connected, the air line branches to the remaining components of both the right and left pneumatic power sections.

Since the remaining components of both sections are identical, a description of only one section will be given. The next component in the air path is a pressure reducer and regulator valve (labeled ADJUST) which sets the air pressure distal to it. This working air pressure is indicated on a 0-30 pounds per square inch pressure gauge (labeled PRESSURE). The range in which the ventricles are normally operated is from four to 12 pounds per square inch. However, these relatively high pressures (207 to 620 mm. Hg) do not appear in the air chamber of the artificial ventricle.

Next in this series is the three-way electromagnetic solenoid valve whose operation is governed by the rate, duty cycle (MSMV), and solenoid driver circuits. In its unenergized position, the solenoid valve blocks air pressure at point A and provides an open air path from B to C. In this position, the air in the ventricle is vented to the

surrounding atmosphere and the ventricle refills with liquid. When the solenoid valve is electrically energized, the exhaust port C is closed and there is an open air path from A to B. With the solenoid valve in this position a pulse of pressurized air is sent along three paths -- to the artificial ventricle and to the surrounding atmosphere by way of two air bleed-off valves. These adjustable needle valves are labeled MANUAL and CONTROL VALVE in Figure 21. The MANUAL valve provides a limited amount of fine control over the action of the CONTROL VALVE.

In normal operation of the power unit the MANUAL valve is usually closed and the ADJUST control is initially set to obtain an adequate operating point. Then the CONTROL VALVE (actuated by the motor in the automatic control system) alters the ventricular air pressure around the initial setting. This latter action is in part responsible for determining the liquid output of the artificial ventricle.

A photograph of the front panel of the rack-mounted pressure control module is shown in Figure 22. In addition to housing the air pressure controls and gauges mentioned above, this module also contains the motors of the automatic control system and various lamps which indicate the status of the control motors. The air pressure output connectors to the artificial ventricles are at the bottom center of the panel. A Model II ventricle is seen attached to one of these connectors.

A photograph of the back of the pressure control module is shown in Figure 23. The electromagnetic solenoids (labeled SOL), control motors (labeled MOTOR), and the automatically-controlled needle valves (labeled CONTROL VALVE) are easily seen. The air pressure input to the module is through the long ribbed hose in the center of the chassis. Other interconnecting air lines are evident in the photograph. The terminal blocks on the right and left edges of the chassis are for electrical connections to the solenoids and control motors respectively.

All of the electronic circuits associated with the power system utilize solid-state devices. The basic rate of each ventricle is determined by means of a relaxation oscillator circuit employing a unijunction transistor (47). The rate can be varied from 15 to 240 pulses per minute. The wide range in pulse rate was chosen to encompass not only normal heart rates but also very fast and slow rates for in vitro testing purposes.

The oscillator pulses are fed into a three-transistor monostable multivibrator (MSMV) circuit (47). This circuit provides one output pulse for each pulse received at its input. The output pulse width is variable from 0.2 to 3.0 seconds. Thus, the duty cycle (or percent "on" time) of the MSMV circuit's output pulses is variable from five to 75 percent (at a rate of 15 pulses per minute) or from 80 to 100 percent (at a rate of 240 pulses per minute). At a

normal rate of 70 pulses per minute the duty cycle can be varied from  $23 \frac{1}{3}$  to 100 percent. Relatively long duty cycles permit the possibility of having a programmed pressure wave applied to an artificial ventricle.

Another circuit in the device can be switched into operation to take the place of the previously described rate and MSMV circuits. This is a variable frequency, variable ratio pulse generator circuit (47). The rate is variable from 20 to 200 pulses per minute and the duty cycle, at any pulse rate, is variable from 0 to 100 percent. Thus either one of the two parameters can be set and will remain constant as the other parameter is varied. This circuit, when switched into use, operates both solenoid valves simultaneously at the set rate and set duty cycle. This circuit is most useful when two ventricles are being driven.

The output pulses of either the above circuit or the MSMV circuit are fed to a solenoid driver circuit which utilizes a silicon controlled rectifier. The solenoid, then, meters the compressed air to and from the artificial ventricle as described earlier. Other than the potentiometers and switches, the solenoid valves (one per ventricle) are the only components of the power system which are subject to mechanical wear.

The power system is extremely versatile in that two artificial ventricles can operate either in unison (with or without identical duty cycles) or asynchronously at the same

or at different rates (again with or without identical duty cycles). Pushbuttons are provided both for manual operation of each ventricle individually or together and for the independent stopping of each ventricle if necessary. Visual and aural indications are given for each "beat" of each ventricle and meter indications are provided for quick determination of both rate and duty cycle. Provision has also been made for accepting an external rate signal, for example, the atrial electromyogram of a deventricularized heart or the limb electrocardiogram of an animal with a bypassed normal heart. These electrical rate signals constitute other possible means of artificial ventricle regulation by feedback control. Figure 24 is a photograph of the module which contains the rate and duty cycle circuits, switches, and indicators along with several electronic power supplies for other modules of the overall system.

There are four parameters which can be adjusted to alter the liquid output of the artificial ventricle: 1) the pressure of the pulses of compressed air; 2) the duty cycle (fraction of entire cycle during which air enters the ventricle); 3) the air bleed-off rate in the pulsed air line; and 4) the pulse frequency. In this study automatic adjustment of the third parameter regulated the stroke volume in response to an animal's changing circulatory needs. When the entire system was first put into operation, the rate, duty cycle, and working air pressure of the ventricle were

adjusted to give a satisfactory blood pressure and flow rate. These adjustments, then, usually remained fixed. Then the control system took over the function of keeping the blood pressure in the input line of the artificial ventricle within a predetermined reference zone.

An actual air pressure waveshape taken at the base of a Model II ventricle during a right ventricular bypass experiment on a dog is shown in Channel 6 of the recording reproduced in Figure 25. This waveform was measured by means of a strain gauge pressure transducer <sup>1</sup> connected to the air chamber of the ventricle by a short air-filled cannula. There is some distortion to the air pressure tracing since the pressure-proportional electrical signal was capacitively coupled to the recorder. The resulting waveforms of both the pulmonary arterial blood pressure (Channel 2) and the relative blood flow through the artificial ventricle (Channel 5) are also shown in this recording.

The shape of the air pressure waveform suggests that it is simply a periodic train of rectangular pulses. However, the actual waveform can be modified by many factors: 1) the load imposed upon the pneumatic power system by the artificial ventricle; 2) the settings of the various air bleed-off valves and the regulator-reducer valve; 3) the

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<sup>1</sup>Statham PR23AC, Statham Instruments, Incorporated, Hato Rey, Puerto Rico.

diameters and lengths of the tubing used in the pneumatic circuit; 4) the orifice sizes of the solenoid valve and the speed with which the valve opens and closes; 5) the pressure reserve of the compressed air supply; and 6) the density of the gas used.

No attempts were made to produce a particular air pressure waveshape. The pneumatic power system could be improved by utilizing an air pressure waveform shaping device. Studies could then be conducted to investigate the effects of various air pressure waveforms upon systemic and pulmonary arterial blood pressure and blood flow waveforms. An increase in the rise time of the air pressure pulse would result not only in lower accelerative forces being impressed upon the blood in the ventricle but also in lower peak blood pressures in the outflow line. Blood trauma, as well as inertial movements of the ventricle itself, may occur if the air pressure increases too abruptly. Another desirable feature would be the incorporation of a negative pressure adaptor to assist the diaphragm of the artificial ventricle during the filling phase. Waveshaping devices have been developed and utilized (58). Kolff et al. (66) produced an instrument to study the effects of various air pulse waveshapes upon an animal's actual arterial blood pressure. They found that an h-shaped air pressure waveform produced the most natural arterial blood pressure waveform.

### The Automatic Control System

Concurrent with the development of the pneumatic power system, a feedback control system was designed to automatically adjust the liquid output of the artificial ventricle. Briefly, the control system altered the ventricle's stroke volume (and thus its liquid output) in response to changes in pressure in the ventricle's liquid input line. By this means, the control system was sensitive to changing requirements of an experimental animal's circulatory system. Input line pressure (similar to atrial pressure) was selected as the controlling parameter since this variable has been found to be a significant factor in normal heart regulation and in other artificial ventricle control systems and it is easily measured (24, 58, 66, 98, 112, 121).

Some basic considerations of this pressure servomechanism are worth briefly noting. Being a feedback system it is immune to many shortcomings of open loop systems since the input knows what the output is doing (but possibly not immediately) and makes any necessary corrections. It is reasonably immune to alterations in valve friction, tubing size, air pressure, and other difficulties which affect the forward path (59). However, it has a low tolerance to difficulties in the feedback path. Thus the necessity of a reliable feedback path is obvious.

The liquid input line pressure was converted to a



voltage to which the control system was actually responsive. If the pressure-proportional voltage left a preset reference zone, a motor-valve assembly was activated. This assembly altered the air pressure available to the artificial ventricle and thus the ventricle's stroke volume.

Following the fabrication of the control system, two artificial ventricles (Model II) and the power and the control systems were integrated to produce a semiautomatically-controlled two-chambered artificial heart which had a variable stroke volume and a fixed pulse rate.

The operation and components of the control system will be described with reference to Figure 26. This figure is a block diagram depicting a one-ventricle control system in relation to the cardiovascular system. Depending on the animal procedure being used to test the system, the pressure signal was taken from the right atrium (or vena cavae) or from the left atrium. In any event, the chosen pressure corresponded to that in the liquid input line of the artificial ventricle.

The pressure transducer used was a Statham<sup>1</sup> PR23-1D-300 differential type with a range of -50 to +50 mm. Hg. This is a strain gauge transducer with four active arms in a Wheatstone bridge configuration. The frequency response of

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<sup>1</sup> Statham Instruments, Incorporated, Hato Rey, Puerto Rico.

the transducer is essentially flat from zero to 20 cycles per second thus making it quite adequate for its purpose (122). The transducer was powered from a ten volt power supply and was connected to the liquid input line of the artificial ventricle by a small liquid-filled catheter. Care was taken to assure that the transducer's pressure-sensitive diaphragm was at the same level as the desired point of pressure measurement in the artificial ventricle. The transducer's electrical signal was amplified by a small solid-state, fixed-gain operational amplifier.<sup>1</sup> The output of this amplifier was made available for recording purposes.

The disadvantage to this means of pressure measurement was in the use of a large external transducer and its accompanying catheter. The inclusion of a small and accurate pressure transducer in the artificial ventricle would be advantageous. Any measurement error due to position and/or movement would then be reduced to a minimum. A small (1/4 inch diameter x 1/4 inch thick) pressure transducer<sup>2</sup> which used resistive paint was tested for use. This unit had several advantages other than its small size: 1) large output voltage change per unit change in pressure; 2) very

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<sup>1</sup>Model 106C, Analog Devices Incorporated, Cambridge, Massachusetts.

<sup>2</sup>Model CS-1-54M, Clark Electronic Laboratories, Palm Springs, California.

simple circuitry needed; and 3) low cost. The transducer showed good sensitivity and response time but lacked good repeatability and was sensitive to mechanical vibration. Higher priced units are commercially available, however, which have comparable specifications to the Statham transducer.

Next in the signal path (Figure 26) was the highly essential indicating and main controlling mechanism -- a double set-point 0-1 milliampere d-c meter relay.<sup>1</sup> The pressure-proportional voltage signal (heavily damped to suppress transients) was continuously indicated on this meter. The meter relay not only made possible an easy and exact initial calibration procedure but also provided a visual display of pressure regulation.

Continuous error correction of liquid input line pressure was not possible since the upper- and lower-limit detectors of the meter relay gave the control system an adjustable "dead" zone. The use of a reference or "dead" zone allowed small and normal pressure variations (those due to respiration) to occur without control circuit activation. Thus the control system was inoperative when the artificial ventricle's liquid output was adequate enough to assure the maintenance of the chosen pressure reference zone.

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<sup>1</sup>Model 502-L, API Instruments Company, Chesterland, Ohio.

The upper and lower limits of the pressure reference zone could be easily and quickly set anywhere within a maximum pressure range of 40 mm. Hg and the reference zone could be as small as 0.24 mm. Hg. Normally the meter was calibrated so that mid-scale (0.5 milliampere) corresponded to zero mm. Hg, zero milliamperes corresponded to "-x" mm. Hg, and 1.0 milliampere corresponded to "+x" mm. Hg.

The upper- and lower-limit switching functions of the meter relay determined the direction of current in the control motor's armature and thus its direction of rotation. The control motor was a small separately-excited shunt-wound d-c unit.<sup>1</sup> Its field was continually excited by a 27 volt d-c supply while a separate 0 to 35 volt d-c supply provided the armature voltage. The speed of the output shaft of the control motor was variable from zero to 30 revolutions per minute. Thus the error-correcting response time of the control system could be varied simply by changing the speed of the control motor. The motor was connected to the air bleed-off CONTROL VALVE of the pneumatic system. This valve was responsible for controlling the stroke volume of the artificial ventricle.

Figure 27 is a photograph of the control motor power supply module which can drive two motors. The relays (two

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<sup>1</sup>Type B-9-1, John Oster Manufacturing Company, Genoa, Illinois.

DPDT types per motor) which control the current direction in the armature are at the top of the module. The black knobs set the desired motor speed. The other switches allow either for automatic operation or for manual operation with control over the direction of armature rotation. The meter provides an indication of relative motor speed (30 revolutions per minute = maximum speed = 1.0).

Figure 28 is a photograph of the module which contains the meter relays and the necessary electronics for both powering the pressure transducers and processing their signals. The Statham pressure transducer is also shown in the photograph. The pressure reference zone is determined by the settings of the thick meter pointers. The accompanying electronics for the meter relays are located in another module (Figure 24). The meter relay module is a completely self-contained unit (except for a-c power) as far as pressure measurement is concerned and can be used as a two-pressure monitor for any surgical procedure.

The remaining components of the two-ventricle control system are shown in Figures 22 and 23. The module shown in these two figures has been described earlier. The latter figure shows the air bleed-off valves (labeled CONTROL VALVE) at the rear of the chassis. To permit a linear displacement of the CONTROL VALVE shaft, this shaft was connected to the control motor shaft by a six-inch flexible coupling. The various lamps (labeled INC, DEC, A, B, C, and D) seen in

Figure 22 indicate both when the control motor is operating and what it is attempting to do. The RESET button reverses the direction of control motor rotation -- an event which becomes necessary when the CONTROL VALVE reaches either its fully closed or fully opened position.

The control system is a regulator type (as opposed to a follower type) since its purpose is the regulation of the liquid pressure in the artificial ventricle's input line within a set range regardless of any fluctuations that occur as a result of external disturbances (84). The reference input, which is the "signal" established as a standard of comparison for the feedback control system, is determined by the limit markers on the meter relay. The directly controlled variable is the liquid input line pressure since it is directly measured and controlled. The stroke volume of the artificial ventricle is actually an indirectly controlled variable even though it constitutes the output of the entire system. The stroke volume could also be called the output forcing function.

This is a closed-loop control system since it contains a feedback loop and corrective effort is determined by both the desired value and the actual value of the controlled variable. Negative feedback is utilized to cause the influence of a disturbance to the regulator to be minimized so that the system maintains, within limits, a constant liquid input line pressure. Also the controller is a continuous

system as opposed to a sampled-data system.

Finally the control system is subject to further subdivision due to the relationship between the output forcing function (stroke volume) and the actuating or error signal (abnormal liquid input line pressure deviation). The system is called a maximum-effort type of controller (84, 85). The maximum-effort principle is an intentional use of nonlinearity. It is a nonlinear system since there is no tendency for the relationship between the output and input to be a constant. A linear controller grades its output in proportion to the error signal (and possibly also to its derivatives and integrals). The linear design therefore arises from an error-oriented viewpoint. The maximum-effort viewpoint, however, is energy-oriented and involves using all available effort to counteract an error whenever corrective action is called for. In other words, when the error signal leaves a preset range, the control system switches in a set amount of power to drive the controlled variable back toward its chosen setting.

To better illustrate this regulator's degree of fine control over a measured variable, several simple control systems will be described. With reference to Figure 29, part a shows a simple on-off response to a measured parameter, such as turning on room lamps when the sun goes behind a cloud. There is no regulation of the measured parameter and there is no feedback. Part b represents the usual home-

heating system where feedback is combined with on-off response. The furnace goes on if the room temperature falls below the desired control point. However the room temperature may climb much higher than desired since no cooling is provided. The system of part c provides both heating and cooling and could represent the temperature control of a water bath. Note that the rate of heating or cooling is reduced as the control point is approached. The control problem of part d is the same as that of part c except that two modifications have been incorporated to improve the speed and accuracy of the system's response. Heating and cooling now operate at a constant rate when called for. This is the maximum-effort response. However, in addition a computer measures the time derivative of the controlled parameter, takes account of the lag time in the temperature-recording device, and shuts off the heating or cooling before the control point is reached. Thus oscillation of the system is quickly damped. Another way to minimize the "hunting" action is the use a "bang-bang" controller in which maximum positive effort alternates with maximum negative effort in the same cycle (85).

The transfer function for the maximum-effort regulator of the artificial ventricle's control system is shown in Figure 30. Note that there is a wide degree of adjustment possible in several variables: 1) the chosen optimum fluid pressure (P); 2) the width of the pressure reference zone



(W); and 3) the degree of effort (h) to be expended (actually control motor speed). The point P does not necessarily have to be in the center of the pressure reference zone. For the control system built in this study, the magnitude of the effort exerted is independent of the direction of the error present, i.e.,  $|h_-| = |h_+|$ . The alternate case,  $|h_-| \neq |h_+|$ , would be necessary if, for example, a positive error were to be weighted more than a negative error.

The pressure reference zone (in Figure 30) could be compressed to a single vertical line but then the control system would be trying to correct for small and continual variations. These corrections are unnecessary since small pressure variations (respiratory modulation) are normal and do not constitute detrimental errors. Thus the control system cannot "fight" with the animal in trying to alter these normally occurring variations. The zero-width reference zone control system is briefly discussed by Merriam (83). He also demonstrated that, in general, when only response errors are weighted in an error measure (i.e., the control effort is not weighted), the optimum controller is always of the maximum-effort variety.

The actual optimization of the artificial ventricle's control system is an attractive idea but no such attempt to do so was undertaken. The underlying concept of optimization is quite simple: generate a signal that will vary the control settings for the process in such a way that a selected

performance index stays at an optimum value despite random variations in any factors that affect the process (84).

There are two disadvantages to the maximum-effort control system. One is that it has a tendency to hunt around the zero signal level. However, this is, in part, a function of the width of the reference zone. The other is that in systems with time constants it is not easy to predict the proper moment to switch off the actuator in order to prevent overshoot. The experimental performance of the control system will be discussed in a later section. However, it should be pointed out now that results of animal trials indicated that the pressure-responsive control system often exhibited a hunting response. It appeared that the animal's response time<sup>1</sup> was relatively long. In other words, the input (reference zone on meter relay) did not know what the output forcing function was doing until a significant amount of time later. The hunting response was minimized by using a small rate of change in error correction, i.e., a relatively small magnitude of effort  $h$ . The problem could also possibly be alleviated by incorporating a sampling network into the control system.

Although only one pressure signal was used as a

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<sup>1</sup>The response time of the animal can be considered to be the interval of time between a change in artificial ventricular stroke volume and the resulting change in liquid input line pressure.

controlling parameter, there was no guarantee that it provided the best match with the animal's remaining control systems (which include various vascular and respiratory reflexes). Much work needs to be done on matching these remaining regulatory mechanisms of the experimental animal to the inanimate control and power systems associated with the artificial ventricles. It may be necessary to have a rapid response to and a rapid correction of small errors, or, quick error response with slow correction may be a better combination. Another possibility would be to have a slow (or delayed) response to an error along with either a fast or a slow rate of error correction. It is very likely that various combinations of responses and corrections may prove to be optimal. A comprehensive study not only of other selected functional cardiopulmonary variables but also of various response-correction combinations should be undertaken, with the goal of determining which one or combination of variables would best reflect the circulatory requirements of the body and activate the control mechanism.

More important, it might be desirable to incorporate into the system the capability of response to multiple input signals. With several physiologic signals as possible feedback parameters, it is apparent that some sort of logic system would be desirable in order to make optimum use of the available physiologic information. A logic system, given the parameters and their limits, could decide which parameter

should do the controlling and under what circumstances it should dominate. Alternately, combinational control of the artificial ventricle might be advantageous. By this means, several different functions of the artificial ventricle (rate, duty cycle, air pressure rise time, etc.) would be controlled by separate feedback parameters. This might allow the regulatory system to more closely approximate the natural heart's mechanisms for control.

Consideration should also be given to means which will assure equal blood flow from both right and left ventricles or which will continuously minimize their time-integrated flow differences. The scheme of pressure sensing used in this control system does give an indication of flow balance. If a flow imbalance develops over a short period of time, the liquid input line pressure of the artificial ventricle changes. The control system senses this change in pressure and acts to correct it. The correction also alters the blood flow rate and thus tends to suppress the flow imbalance (providing vascular resistance does not change appreciably). Simultaneous pressure and flow measurements need to be made to completely validate this action.

It can be appreciated that the use of biochemical parameters might more accurately reflect the varying metabolic needs of the tissues. The use of both arterial and venous oxyhemoglobin concentrations as feedback parameters has been attempted with the system described in this dissertation

(34, 35, 41, 42). Satisfactory control (in a dual ventricular bypass experiment) was attained by using venous oxyhemoglobin concentration to control the right artificial ventricle and by using left atrial pressure to control the left artificial ventricle. The advantage of using this combination of control parameters was that one (oxyhemoglobin concentration) insured that the blood flow met the metabolic requirements of the tissues, while the other (atrial pressure) tended to assure the proper distribution of circulating blood volume.

Finally such factors as the amplitude, duration, and frequency of the electrocardiogram's P-wave might possibly be utilized in the regulation of the artificial ventricle. The atrial contribution to the electrocardiogram signal is a manifestation of central nervous system moderator activity. The surgical attachment of the implantable artificial ventricle, as is contemplated in future experiments in this research, is such that the atria will remain intact and, hopefully, viable. If the electrical signal remains active and coordinated with circulatory needs, it would make an ideal feedback parameter to control the "heart" rate of an artificial ventricle.

## EXPERIMENTAL RESULTS

In Vivo Experiments

Both in vivo (animal) and in vitro (bench) experiments were conducted to evaluate the artificial ventricles, the pneumatic power system, and the automatic control system. These experiments were done in order to properly test the entire device's overall quality as a normal heart substitute. Once a few preliminary bench tests were performed on an inanimate model of the circulatory system, in vivo studies with the device were conducted. Due to the testing sequence adopted, a large number of maneuvers were carried out on animals before they were done on the circulatory model. The animal experiments not only gave a better insight into the operation of the complete device, but also led to several observations which were later attempted on the external circulatory model. For these reasons, the animal experiments will be described first.

Evaluation of all components in the artificial ventricle system was through the use of the dog as the experimental animal. Dogs were used in the acute studies mainly because of their availability, cardiovascular anatomy, and ease of handling. All animals utilized in this research were handled and cared for in the manner described in "Principles in the Care and Use of Experimental Animals in the College of Veterinary Medicine, Iowa State University."

A team consisting of two or three surgeons, an engineer, a medical technologist, and an instrumentation technician performed the experimental trials. In these procedures 32 dogs weighing from 15 to 40 kilograms were used. They were anesthetized by giving sodium pentobarbital intravenously to attain surgical anesthesia. Intermittent positive pressure ventilation was maintained by using a commercial respirator.<sup>1</sup> Ventilation rate for the anesthetized animals was about 200 milliliters of oxygen per kilogram per minute (81).

The in vivo testing involved the development and utilization of three types of short-term, open-chest procedures. Since the goal of the project was to develop a successful system, the protocol for each procedure varied from one experiment to the next because it incorporated changes suggested from the results of earlier trials. The three procedures used were 1) total cardiopulmonary (heart-lung) bypass, 2) right ventricular bypass, and 3) left ventricular bypass. (Dual ventricular bypass experiments were performed on 33 dogs using this system in conjunction with another project (34, 41). In these procedures, both right and left natural ventricles were surgically removed and circulation was maintained using the Model II ventricles.) Generally a

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<sup>1</sup>Prothoracic PR-3 respirator. Professional Veterinary Supply, Miami, Florida.

fixed artificial heart rate of 80 beats per minute was employed and  $33 \frac{1}{3}$  percent of the pumping cycle was systole.

The majority of the in vivo trials were individual right and left ventricular bypasses. In these procedures, the natural ventricles were bypassed but left intact and did not pump blood (except for flow into the coronary circulation from the left ventricle). The lungs oxygenated the blood.

The Model II artificial ventricles were located extracorporeally in all experiments and were connected to the animal's vascular system with short lengths of polyvinyl chloride tubing. The connections used were from the right auricle (or vena cavae) to the right artificial ventricle and then to the pulmonary artery. The blood from the left auricle was passed through the left artificial ventricle and into the aorta (or femoral arteries). Each artificial ventricle was used interchangeably in these trials. A series of surgical procedures was first required to establish these techniques as standard test methods.

Naturally open-chest experiments do not impose normal operating conditions on the animal's cardiovascular system since the pressures in the thorax are obviously altered. To get optimum performance from an anesthetized animal, the chest should be closed. This will also reduce the susceptibility to surgical shock. However, open-chest trials naturally precede closed-chest trials and the data obtained can be validly related to other types of procedures.



The pumping system (without feedback control) was used effectively in total heart-lung bypass experiments. This preparation was utilized in 12 dogs to evaluate the pumping ability of both the pneumatic power system and the Model II ventricles. Normal flow rates for a dog (at normothermia) of approximately 100 to 400 milliliters per kilogram per minute were sought (20).

A right thoracotomy was performed through the fifth intercostal space. The azygos vein was ligated. Heparin (three milligrams per kilogram of body weight) was given at this time in order to prevent blood coagulation during the ensuing procedures. The pericardial sac was incised and cannulas were inserted into the anterior and posterior vena caval veins through incisions in the wall of the right atrium. Loops of umbilical tape were placed around the vena cavae 1.5 centimeters from the tips of the cannulae. The left femoral artery was cannulated with a relatively large cannula. Catheters were inserted in the right femoral artery and right jugular vein for the purpose of measuring central arterial and venous pressures respectively. By occluding the caval ligatures all systemic venous blood, except that returning through the coronary veins, could be shunted through the extracorporeal circuit.

The total heart-lung bypass procedure is schematically illustrated in Figure 31. The external blood path consisted of a bubble oxygenator, a device for heating or cooling the

blood, and the artificial ventricle. Blood-gas interchange was accomplished by bubbling either 100 percent oxygen or 95 percent oxygen and five percent carbon dioxide through the bubble oxygenator. In these trials, the artificial ventricles performed as well as a commercial finger-type blood pump.

The second procedure used was a right ventricular bypass. This procedure was the primary technique used to evaluate the complete system. In 14 dogs a left thoracotomy was performed through the fourth intercostal space. An intake cannula for the artificial ventricle was placed in the right atrium. A second cannula was inserted in the pulmonary artery through a right ventriculotomy incision. A loose ligature was placed around the pulmonary artery. By tightening this loop around the cannula outflow from the right ventricle was prevented and all the blood entering the right atrium was made to flow through the external circuit. This procedure is shown in Figure 32. The artificial ventricle was evaluated as a replacement for the natural right ventricle using this open-chest technique.

The third procedure involved a left ventricular bypass, and was used in six dogs. The blood shunting technique was similar to that described above, except that the intake cannula for the extracorporeal circuit was placed in the left atrium and the outflow cannula was placed in the right femoral artery. During bypass a clamp was placed on the aorta

downstream from the origin of the coronary arteries, thus blocking aortic blood flow to the periphery. In this procedure the artificial ventricle replaced the function of the natural left ventricle except for furnishing coronary arterial blood flow. This third procedure is illustrated in Figure 33. Bypass techniques in which the individual ventricles were shunted did not require an external blood-gas exchanger since the pulmonary circulation was not interrupted.

In order to evaluate not only the components of the artificial ventricle system but also the condition of the animal, the following parameters were monitored utilizing appropriate transducers and multichannel paper recorders.<sup>1</sup>

1. Electroencephalogram (EEG)
2. Electrocardiogram (EKG)
3. Aortic blood pressure -- strain gauge transducer and fluid-filled cannula
4. Pulmonary arterial blood pressure -- strain gauge transducer and fluid-filled cannula
5. Right atrial blood pressure -- strain gauge transducer and fluid-filled cannula
6. Left atrial blood pressure -- strain gauge transducer and fluid-filled cannula
7. Thoracic esophageal temperature -- thermistor

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<sup>1</sup>Grass Model 5 and Model 7 Polygraphs, Grass Instruments Company, Quincy, Massachusetts.

8. Blood flow rate through the artificial ventricle --  
electromagnetic flowmeter
9. Air pressure waveform in the artificial ventricle --  
strain gauge transducer and air-filled cannula

Note that parameters No. 5 and No. 6 are the signals associated with the automatic control system.

EKG and EEG potentials were monitored because they are sensitive indicators of myocardial and brain function respectively. Deterioration of these signals during the trials could be interpreted as evidence of inadequate oxygenation of these vital tissues.

During each surgical procedure blood biochemical and hematological studies (pH,  $P_{O_2}$ ,  $PCO_2$ , hematocrit, total hemoglobin, and plasma hemoglobin) were also used to evaluate the animal's condition. The blood samples used for gas concentration determinations were refrigerated and then transported to a local hospital for testing following completion of the experimental procedure.

The presurgical bioelectric and blood biochemical and hematological control values for each animal were compared with those values determined during experimentation. It should be mentioned that in trials where maximum survival time is to be sought, additional criteria (physical condition, mental alertness, etc.) might be included in the overall evaluation of the animal-machine combination.

The primary criterion for evaluating the performance

of the artificial ventricle system in the above trials was the ability of the equipment to maintain the animals in as near normal state of homeostasis as possible concomittant with adequate atrial (input line) pressure regulation. In the right ventricular bypass procedures, experimental maneuvers were conducted to vary vena caval blood pressure. Circulating blood volume, one of the determinants of venous pressure, was varied by 1) removing blood, 2) infusing five percent dextrose solution or ten percent dextran in five percent dextrose, and 3) infusing, in single doses or continuously, hypertensive drugs and ganglionic blocking agents. Venous pressures were also momentarily changed by varying intrapulmonic pressure during intermittent positive pressure ventilation. Finally perturbations were induced in a satisfactorily functioning animal preparation by manually altering the fluid output of the artificial ventricle. The control system's function, then, was to restore the animal's altered venous pressure back to its normal level (determined by the limit points on the meter relay) after these changes occurred. The response times of the venous pressure regulating system were of particular importance in these trials.

Figure 34 shows recordings of EKG, pulmonary arterial, systemic arterial, and vena caval blood pressures, relative mean blood flow rate through the artificial ventricle, and EEG taken during a right ventricular bypass test of the system. The hash-marked sections of the time channel

(center recording) indicate intervals in which the control motor was active. The D and I markings indicate attempts of the control system to decrease or increase the vena caval blood pressure respectively. The slow corrections in vena caval blood pressure are easily seen as are similar waveform changes in pulmonary and systemic arterial pressures and artificial ventricular blood flow. In this control sequence, the overcorrecting response of the animal-machine system was due to too fast a response time of the automatic control system. This overcorrecting (or hunting) response can be minimized by matching the control system's response time to that of the animal's. Varying the speed of the control motor conveniently changes the control system's response time. This latter effect is also demonstrated in Figure 34 where the motor speed in the right half of the recording was faster than that in the left half. The various blood pressures and the blood flow show continual change as the CONTROL VALVE varies its position when the control system is operating.

Another example of corrective control sequences with different system response times in a right ventricular bypass procedure is shown in Figure 35. The first and second hash marks on the time channel indicate, respectively, an increase and decrease in control motor speed. The third hash mark indicates where the automatic feature of the control system was turned off. It is easily seen how changes in

control motor speed affect the period and amplitude of the cyclic vena caval blood pressure waveform. Again these cyclic variations are evident in some recorded parameters other than the vena caval blood pressure.

The control system's response to alterations in vena caval blood pressure can also be studied by perturbations to the animal-machine combination such as those shown in Figure 36. In these instances the source air pressure was manually decreased. This caused an immediate decrease in stroke volume of the artificial ventricle which in turn allowed the venous pressure to rise. The increase in venous pressure triggered the control system and within 70 seconds of the onset of the initial change the blood flow and blood pressures were back to their previous levels. The right section of the figure also shows a similar perturbation only with mean levels of some of the parameters being recorded. Again the control system equilibrated the venous pressure within several cycles. The extreme left end of the figure shows expanded recordings of the measured parameters.

During the right ventricular bypass trials it was possible to maintain almost normal systemic arterial pressure and blood flow with only a slight increase in vena caval blood pressure, providing the circulating blood volume was adequate and kept fairly constant. No changes were observed in the waveforms of the EKG and EEG biopotentials during bypass. The preservation of normal waveforms (for the

anesthetic state) inferred adequate oxygenation of those tissues which have high oxygen requirements.

Negative pressure, developed in the input line during the filling phase of the artificial ventricle, often caused the collapse of atrial tissue into the right atrial cannula, thus severely limiting the blood flow. It is possible that this phenomenon is more pronounced in a short-term open-chest trial than it would be in a closed-chest trial using an implanted device. In the latter case, surgical connections to the natural heart would allow the atrial chamber to function more efficiently as a buffer chamber to reduce the pressure gradients occurring between the central veins and the artificial ventricle's blood chamber.

In addition to ventricular bypass experiments, it is important to conduct both ventricular assist studies and total ventricular replacement studies. The circulation pattern in the assistive studies puts two artificial ventricles into parallel operation with the natural ventricles. By controlling the blood flow through the natural ventricles, the blood flow through the artificial ventricles can be varied from zero to full "cardiac" output.

In order to conduct the total replacement studies a method must be developed to attach the proper ports of each artificial ventricle to the aorta, pulmonary artery, and right and left atria. Also a surgical procedure to perform a satisfactory bilateral ventriculectomy is necessary. This



procedure will assure that an adequate portion of the coronary blood supply will be retained to maintain atrial myocardial tissue in a viable state. By not removing the atria, important reflexes from their walls will be preserved and may possibly be utilized as a means of feedback control. Finally a technique must be established for a smooth, flaw-proof conversion from total cardiopulmonary bypass to total implanted artificial ventricular function. The best combination of anesthetic procedures must be determined to minimize depression of the central nervous system and the respiratory and vascular regulatory mechanisms. There is a likelihood that a more efficient external control system is required for an animal preparation lacking the control mechanisms of a natural heart.

Providing that all of the above listed phases were carried out satisfactorily, an artificial ventricle could be implanted using aseptic technique and then evaluated in closed-chest, conscious animals. Cardiovascular studies might include those enumerated above and, when possible, postoperative clinical, clinicopathological, and gross and microscopic tissue evaluations to determine the adequacy of the artificial ventricles.

### In Vitro Experiments

This section is concerned with the performance of a single Model II artificial ventricle and its control system

in conjunction with a specialized test circulation. The response of the ventricle's liquid input line pressure to various disturbances was sought under differing conditions of control motor operation. Water was used for the circulated fluid in all cases.

A diagram of the experimental layout is shown in Figure 37. The output of the artificial ventricle was returned to the constant level reservoir. This reservoir was also supplied with tap water to assure a constant flow from the reservoir regardless of the artificial ventricle's flow rate. The constant level reservoir drained into the ventricle's filling reservoir. The liquid input line pressure (control signal) was proportional to the level ( $h_v$ ) of the water in the filling reservoir above the pressure transducer.

Note that a closed circulation was not used. Since the test circulation possessed no distensibility, there were no temporary storage areas for the liquid. Thus to transfer volumes of liquid, both liquid inflow and outflow tracts were added to the test circulation. Note that since only one ventricle was employed in the test circulation, interaction between two pumps was absent. Naturally this interaction is present in the normal circulatory system.

Even though the test circulation was not closed, the control system did possess a closed loop. In Figure 37 it can be seen that the loop was a combination of electrical, mechanical, pneumatic, and hydraulic elements. The sensing

and control path was composed of the following sections in sequence: liquid input line pressure to the artificial ventricle; pressure transducer; amplifier; meter relay; control motor; air bleed-off control valve; and the artificial ventricle.

Consider the test circulation to be in equilibrium. Then the flow rate through the artificial ventricle is constant and is such that there is no change in the level  $h_v$ . In other words, the artificial ventricle is pumping all that comes to it by way of the constant level reservoir. Into this steady-state condition suppose a perturbation is introduced by a change in any one of the following variables: 1) pulsed air pressure (i.e., stroke volume); 2) flow rate into the filling reservoir; 3) the level  $h_v$ ; or 4) limit markers on the meter relay. Any one of these changes will lead to the establishment of a liquid input line pressure which is outside the chosen pressure reference zone. In other words, an error signal will be generated. The control motor will then be activated and the artificial ventricle's stroke volume will be altered in an attempt to restore the original operating point. By varying the speed of the control motor, with all other variables being held constant, various responses can be obtained and recorded as the control system reacts to the disturbances in the test circulation.

All of the above perturbations were induced into the equilibrated test circulation. In all trials the air bleed-

off control valve was initially set at the same position and the artificial ventricle's rate was 70 beats per minute while its duty cycle was 35 percent. All of the in vitro trials exhibited the same behavior -- the liquid input line pressure showed an oscillatory response with a linearly increasing amplitude. This behavior continued until the air bleed-off control valve reached its fully closed position at which time the control system was automatically deactivated and the trial terminated. Thus the test circulation-control system composite was unstable.

Two recordings will be presented which illustrate the system's response to two perturbations under two different control conditions. The recordings were made on a Grass Model 7 Polygraph at a paper speed of 0.50 millimeters per second. The slow paper speed was the reason that only the envelope of the air pressure waveform is seen.

Figure 38 shows recordings of control motor effort, air pressure at the base of the artificial ventricle, and liquid input line pressure. The two pressures were measured in millimeters of mercury (mm. Hg). In this trial the meter relay was calibrated for a full scale pressure reading of 8.0 mm. Hg (thus the meter's sensitivity was 0.16 mm. Hg per division), the width of the pressure reference zone was 5.0 divisions (0.80 mm. Hg), and the relative motor speed was 0.20. The meter relay limit markers were set so that the meter indication was in the center of the reference zone in

the steady-state condition.

At the event mark (fourth tracing) both limit markers on the meter relay were increased by three divisions (0.48 mm. Hg). This action simulated a step decrease in the liquid input line pressure. The control system interpreted this event as a condition in which the artificial ventricle's stroke volume was excessive. A reduction in stroke volume was initiated to bring about an increased liquid input line pressure. These events are obvious in all three tracings of Figure 38. The INC and DEC designations indicate, respectively, efforts by the control system to increase and decrease the liquid input line pressure. The unstable growing response (which terminated at the asterisk) is easily seen. Note also that the duration of each individual control effort period was longer than its predecessor.

In an attempt to eliminate the unstable response, intermittent operation of the control motor was next used. A timing circuit allowed the control motor to function for only a percentage of the time whenever an error signal was present (47). The "sampling" rate was adjustable from two to 60 samples per minute and the duration of control motor action was adjustable from 0.5 to 25 seconds. Different settings of these two adjustments, then, could produce control motor duty cycles of 1.67 to 100 percent. The cycling of the timing circuit was independent of the error signal.

Figure 39 shows the result of a trial in which the

sensitivity of the meter relay was 0.16 mm. Hg per division, the pressure reference zone width was three divisions (0.48 mm. Hg), and the relative motor speed was 0.40. The duty cycle of the control motor was 50 percent (five seconds "on" and five seconds "off"). At the event mark a slight decrease in liquid flow rate into the filling reservoir was initiated. The control system interpreted this event as a condition in which the artificial ventricle's stroke volume was excessive. A reduction in stroke volume was initiated to bring about an increase in the liquid input line pressure. Again, these events are obvious in all three traces of the recording as is the resulting unstable growing response.

There are several possible explanations for the unstable responses obtained in these trials:

1. The stroke volume of the artificial ventricle was not a function of its input filling pressure. Thus, with a deactivated control system, the ventricle's liquid flow rate would be stable regardless of the level  $h_v$  (in Figure 37).
2. Only one parameter was utilized as a control signal (liquid input pressure) even though two parameters were varying (liquid input pressure and pulsed air pressure). Thus a return to a stable condition necessitated that both parameters attain their pre-perturbation values simultaneously. It was not sufficient that only the control signal parameter

returned to its initial value.

3. The use of too large a diameter (14 centimeters) filling reservoir caused a considerable degradation in the control system's performance. A pressure reference zone width of five divisions (0.80 mm. Hg) meant that the level  $h_v$  had to change by 1.09 centimeters for the meter indication to travel the width of the zone. Thus with a small ventricular flow imbalance, a significant amount of time was needed to change this level and the control system was not immediately aware of either what or when corrective maneuvers were taking place.

The above results were presented only to show the control system's performance when used with a specific test circulation. Many refinements could have been added to the system such as rate feedback and synchronization of the intermittent control motor operation with the initiation of an error. But since the test circulation itself was not a true model of the normal circulatory system, effort spent on refinements would be of limited value.

## SUMMARY AND CONCLUSIONS

The research described in this dissertation is ultimately directed toward a problem which occurs in heart attack cases, that of adequate treatment for the irreversibly damaged heart. Such a heart is one where partial recovery and healing cannot occur even after temporary assistance by either a heart-lung machine or an artificial intrathoracic bypass pump.

The many technical problems relating to the development of a satisfactory heart substitute have been discussed. These include the use of proper materials which will satisfy both the physiologic and physical requirements imposed by years of uninterrupted service. For portable automatic control, transducers for permanent implantation together with miniaturized circuitry must be designed and optimally utilized. A driving mechanism must be provided to continuously energize the artificial heart. The intrathoracic pump must minimize heat production to levels which are safe and tolerable by the body. Finally, an energy source which is portable, reliable, and powerful must be provided. Significant advances in all the above-mentioned areas will open new possibilities of sustaining useful and productive life in certain selected clinical cases of otherwise fatal heart disease.

The design and performance of the artificial ventricles and the power and control systems developed in this research



have been described. The limitations of the system were mentioned along with recommendations for improvement. Both in vivo and in vitro experiments were conducted with the in vivo trials being the ultimate tests for adequate performance. The main emphasis in the in vivo experiments was on the performance of the entire system in short-term animal trials. Long-term animal survival was not sought. The in vitro experiments were conducted to determine some capabilities of the overall system.

The results of automatic control of an artificial ventricle using a single physiologic parameter were, for the most part, encouraging. However, studies should be conducted to compare the relative efficacy of several physiologic events utilized to control single and dual artificial ventricles both in assistive and in total ventricular replacement modes.

It is hoped that this research can contribute both to the investigations of control problem aspects of implantable artificial hearts and to the treatment of the irreversibly damaged human heart. Although many obstacles impede the achievement of total success in this endeavor, the difficulties seem not to be of any greater magnitude than those found as a result of natural heart transplantation.

Finally, to philosophize a little and borrow some words of Willem J. Kolff (64):

"Life might still be acceptable if a vigorous artificial

heart could be supplied, even if two small tubes would have to connect the patient with some kind of pressure system. It is not a solution that any normal man would look forward to, but for the patient in desperate heart failure, what would be the alternative?"

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## ACKNOWLEDGMENTS

The writer wishes to express his sincere appreciation to his major professor, Dr. Neal R. Cholvin for his guidance, assistance, and many helpful suggestions not only in carrying out the writer's research but also in the preparation of this dissertation and for his time spent in the surgery room; to the Iowa State University Engineering Research Institute, the Iowa State University Affiliate Program in Solid State Electronics, the American Heart Association, and the Iowa Heart Association for support in the form of salary, equipment, and supplies; to Drs. Phillip T. Pearson, Howard H. Erickson, Shaheen Al-Nakeeb, and Jess L. Ayers for the many hours spent in the preparation of the experimental animals; to Melvyn Kinney, Randall Mertens, Robert Akins, S. G. Dowell, Cynthia Nelson, Nancyann Nelson, Maria Marchesi, and Barbara Royer for their technical assistance; to Richard Collins and Drs. James H. Magilton and Daniel J. Hillmann for their assistance with the illustrations; and to his parents who enabled him to have the opportunity to undertake this study.

A special appreciation is due to his wife, Anne, not only for her encouragement and patience but also for the time she spent in typing, proofreading, organizing, and assembling this manuscript.

FIGURES

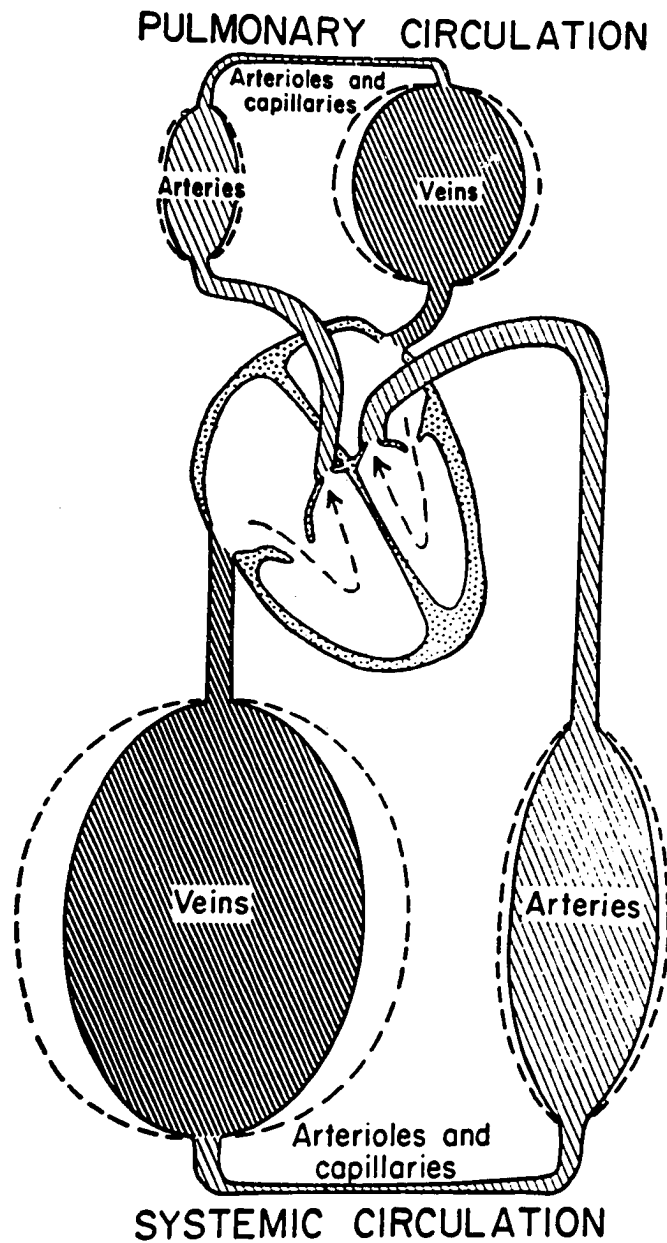


Figure 1. Pictorial diagram of the human circulatory system (Guyton, 52, p. 249)

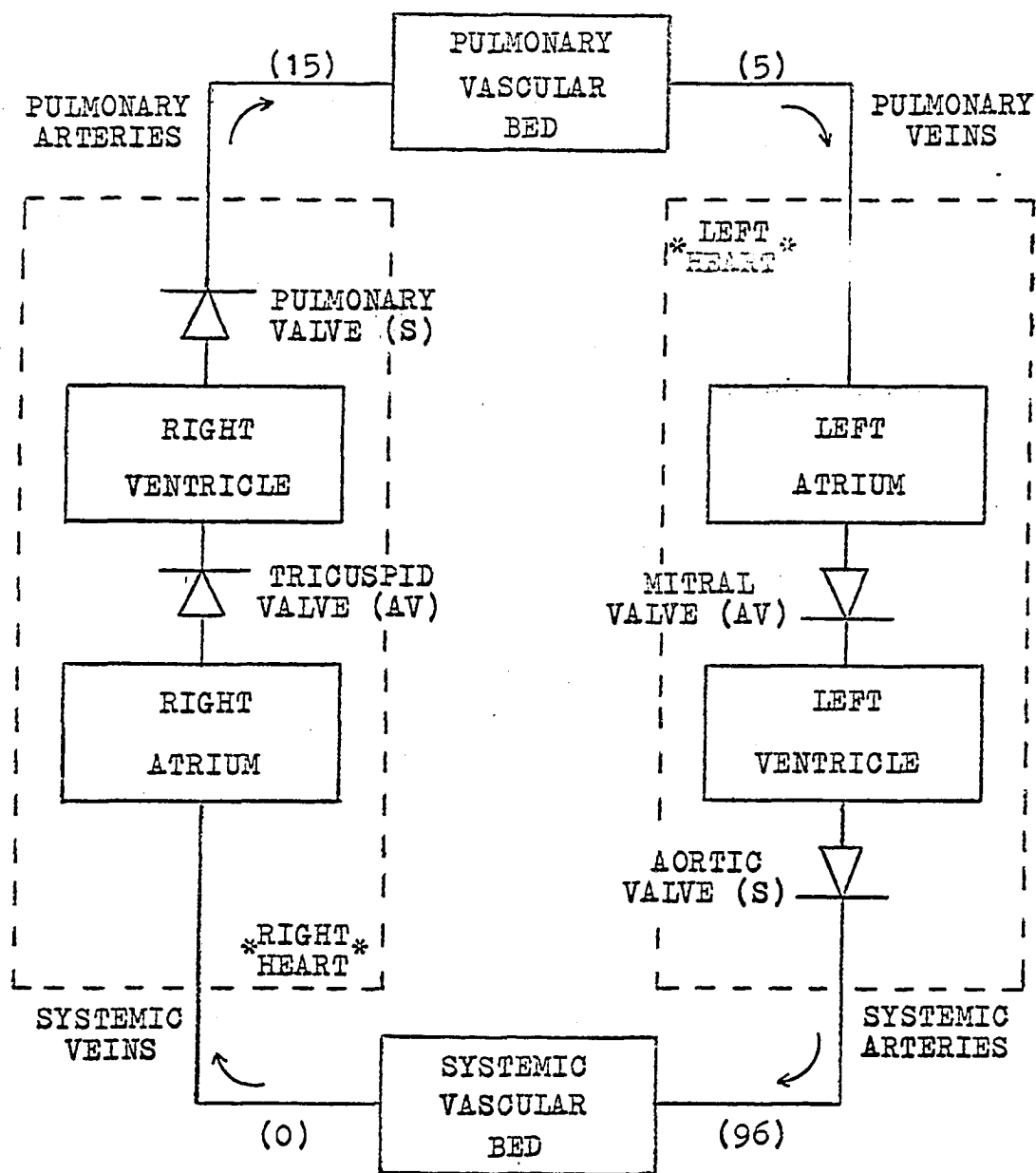


Figure 2. Block diagram of the human and canine cardiovascular system. Number in ( ) is the mean blood pressure in millimeters of mercury. (S) = Semilunar; (AV) = Atrio-ventricular

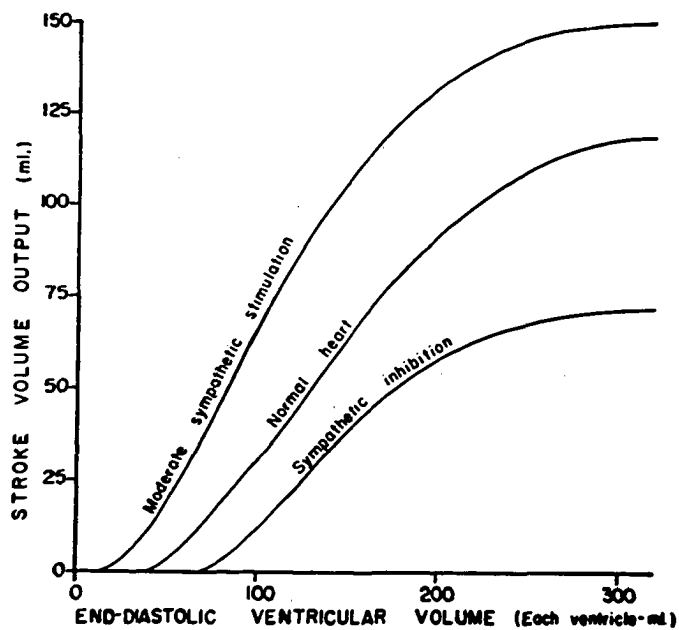


Figure 3. Ventricular function curves (Guyton, 51, p. 336)

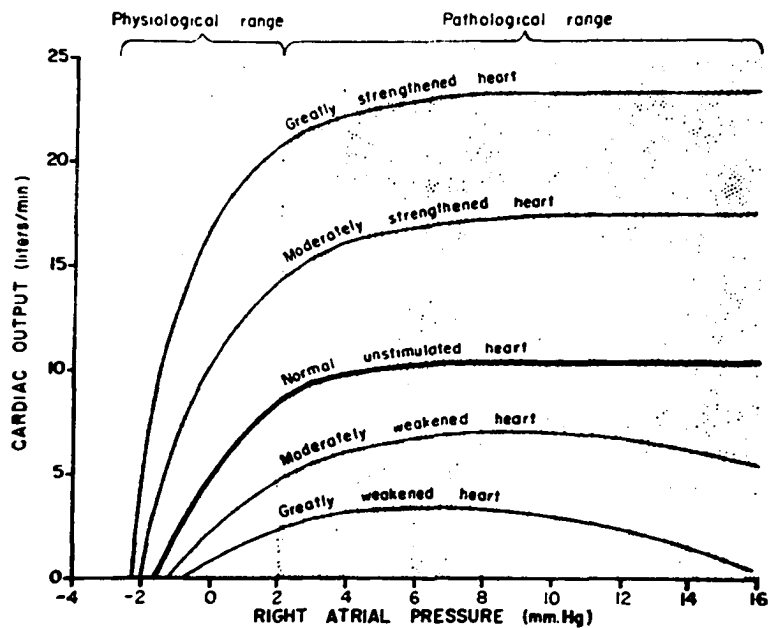


Figure 4. Cardiac output curves (Guyton, 51, p. 456)

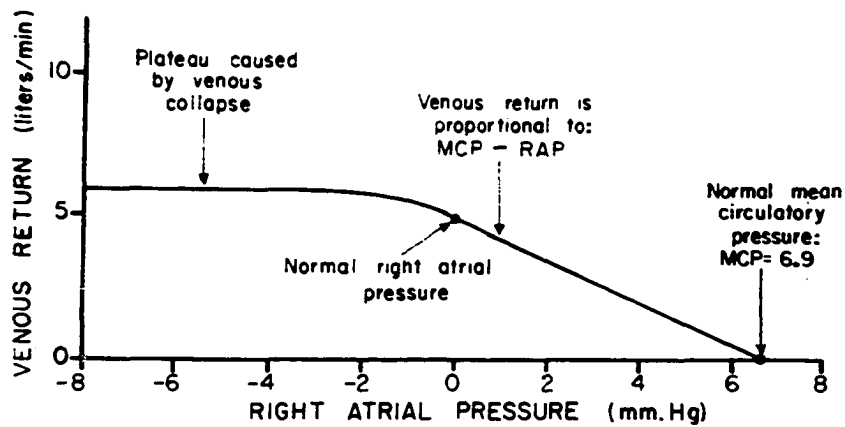


Figure 5. The normal venous return curve (Guyton, 51, p. 457)

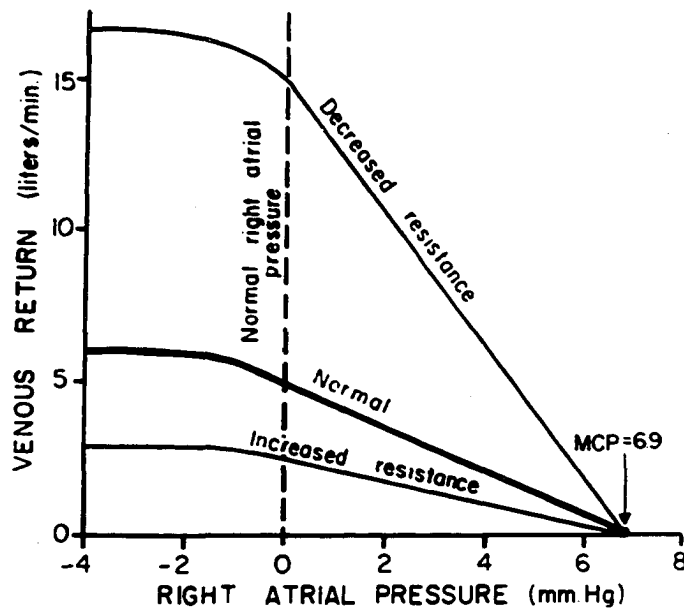


Figure 6. The effect of systemic resistance on the venous return curve (Guyton, 51, p. 458)

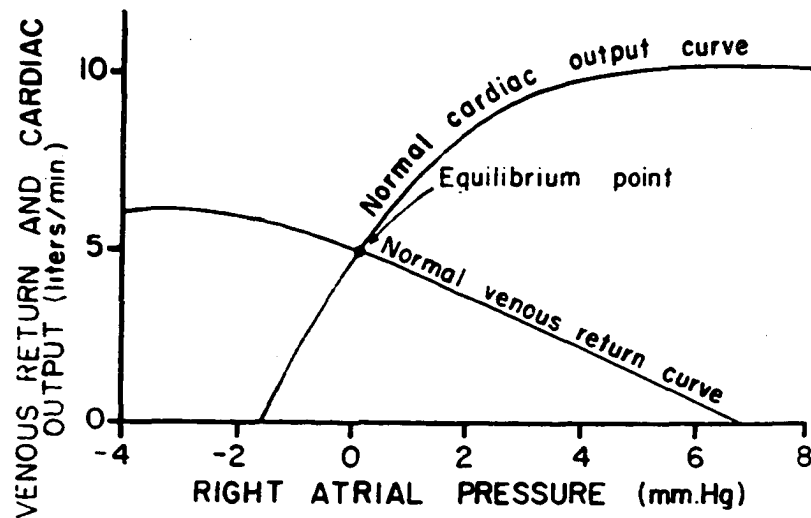


Figure 7. Superposition of the normal cardiac output curve and the normal venous return curve (Guyton, 51, p. 460)

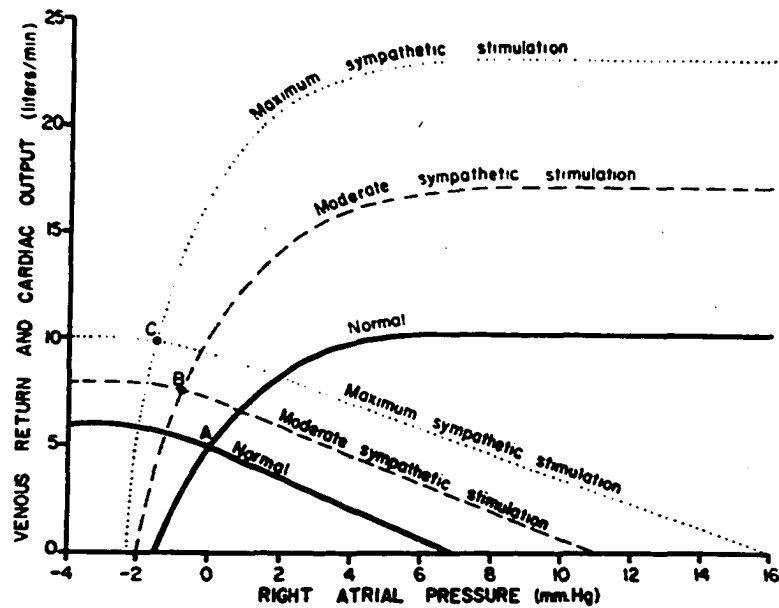


Figure 8. The effect of sympathetic stimulation on venous return, cardiac output, and right atrial pressure (Guyton, 51, p. 461)

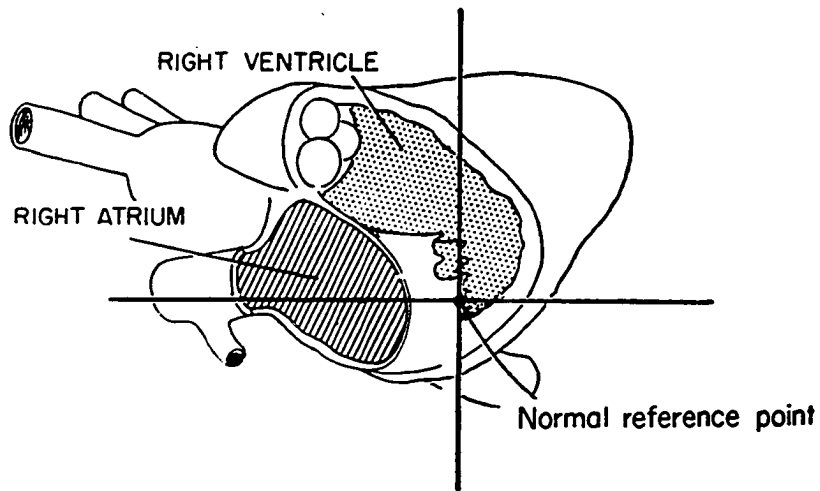


Figure 9. The reference point for pressure measurement (Guyton, 52, p. 274)

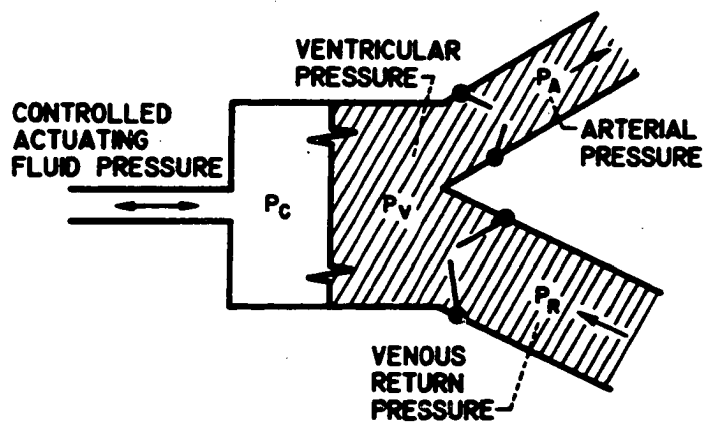


Figure 10. Diagram of a fluid-actuated artificial ventricle (Hiller, et al., 59, p. 129)



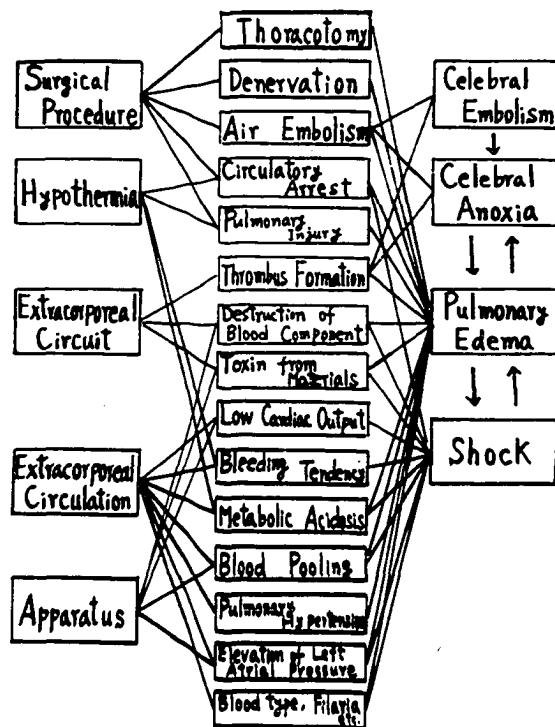


Figure 11. Causes of death in artificial heart experiments (Atsumi, et al., 9, p. 297)

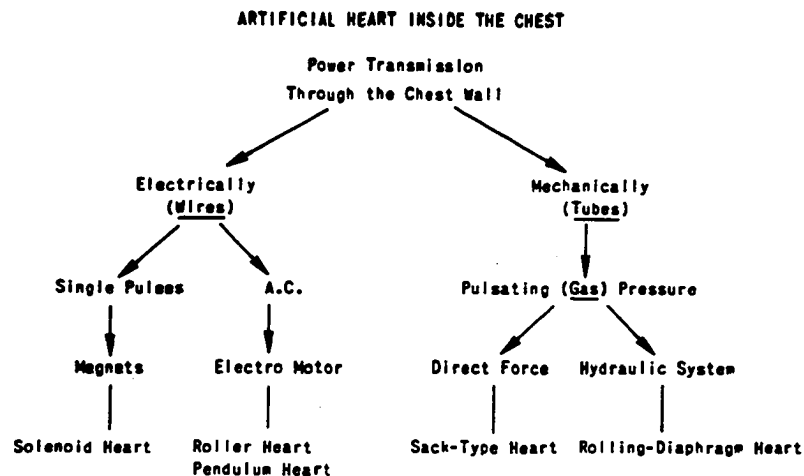


Figure 12. Means of power transmission through the chest wall (Seidel, et al., 110, p. 384)

**CLOSE DUPLICATION OF HEART FUNCTIONS**

Pulse Shaping	Variable Flow Rates
No Suction	Lightweight
Alternate or Simultaneous Pulsing	Low Noise Levels

**EXCELLENT RELIABILITY AND LIFE CHARACTERISTICS**

Low Stress	No Lubrication
Simple Power Supply	Minimal Moving Parts
Negligible Maintenance	

**SIMPLIFIED PACKAGING**

Few Sealing Problems	No Heat Problems
Sufficient Controlled Energy	Easy to Sterilize
Volumetric Efficiency	Flexible Material Selection
Form Factor Flexibility	

**LOW END PRODUCT COST**

Figure 13. Advantages of a fluid amplifier-controlled artificial heart (Barila, et al., 10, p. 32)

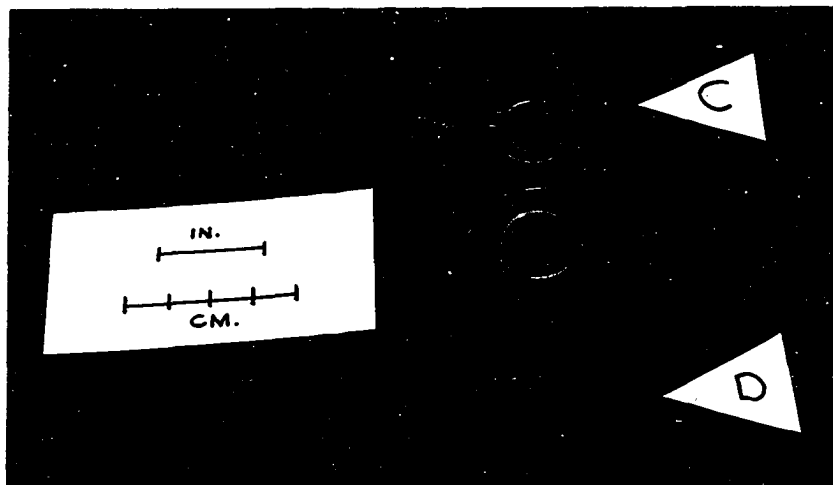


Figure 14. Silicone rubber flap valves for the Model II artificial ventricle; C = flap part, D = seating part

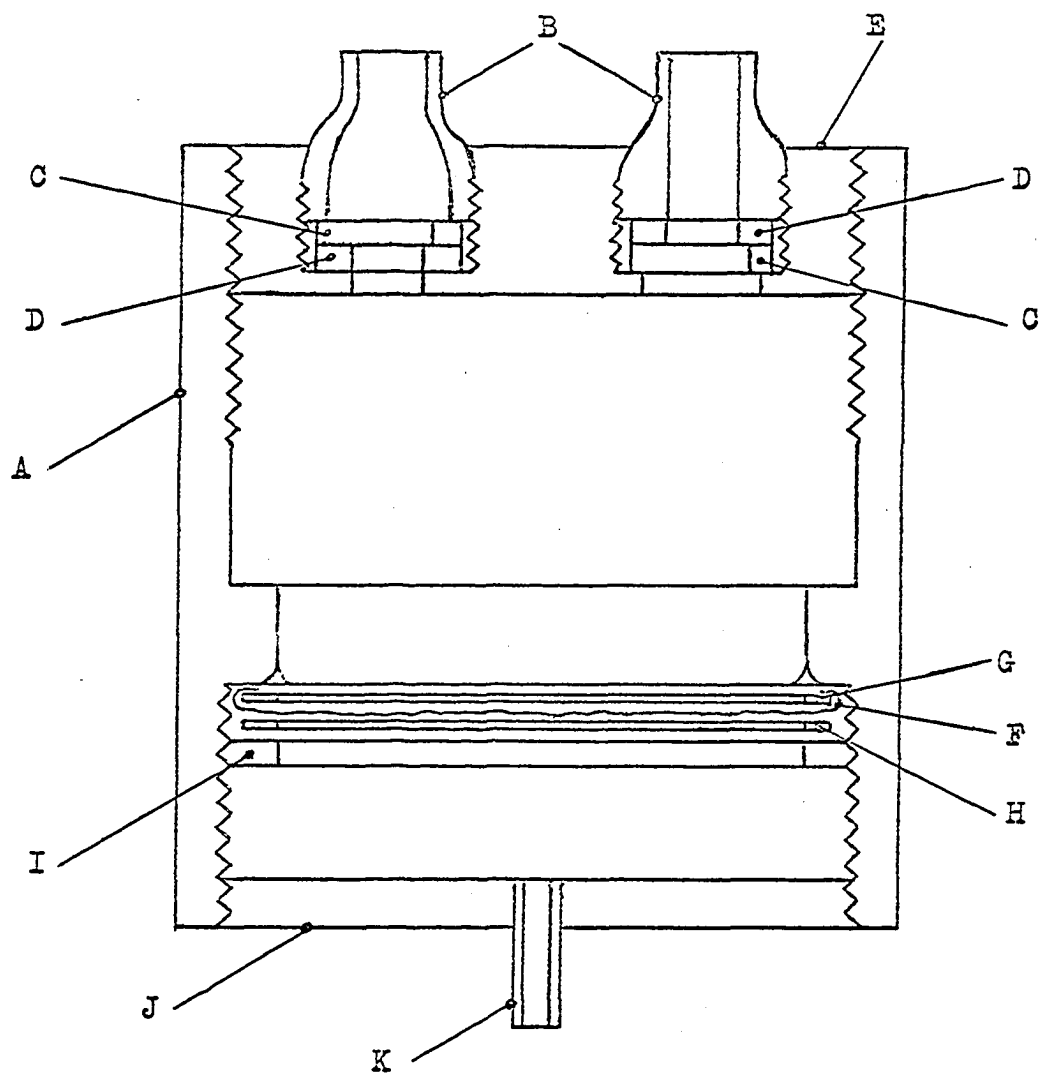


Figure 15. Cross-section view of the Model II artificial ventricle (Letters are explained in the text.)

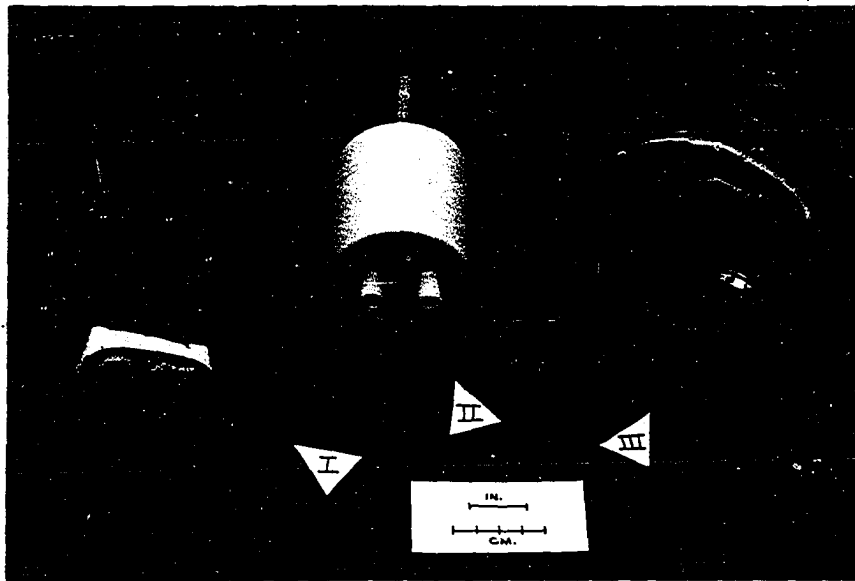


Figure 16. The three artificial ventricles

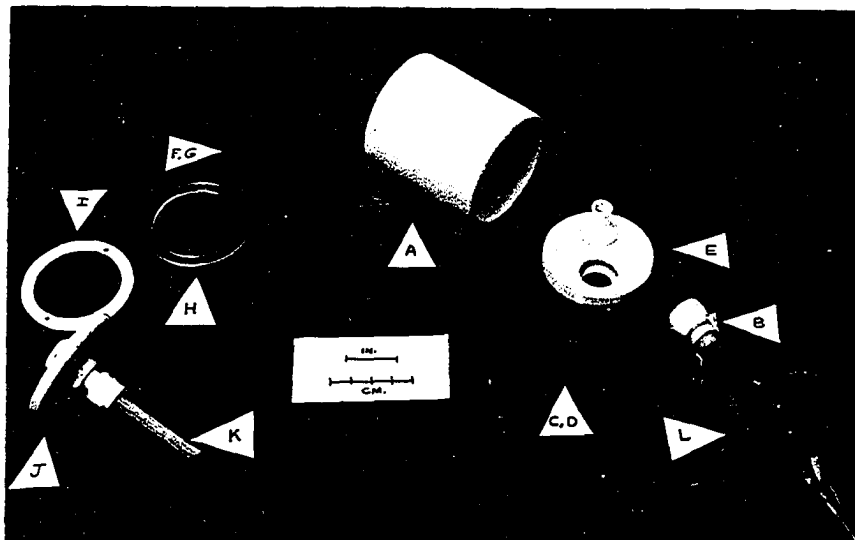


Figure 17. The disassembled Model II artificial ventricle (Letters are explained in the text.)

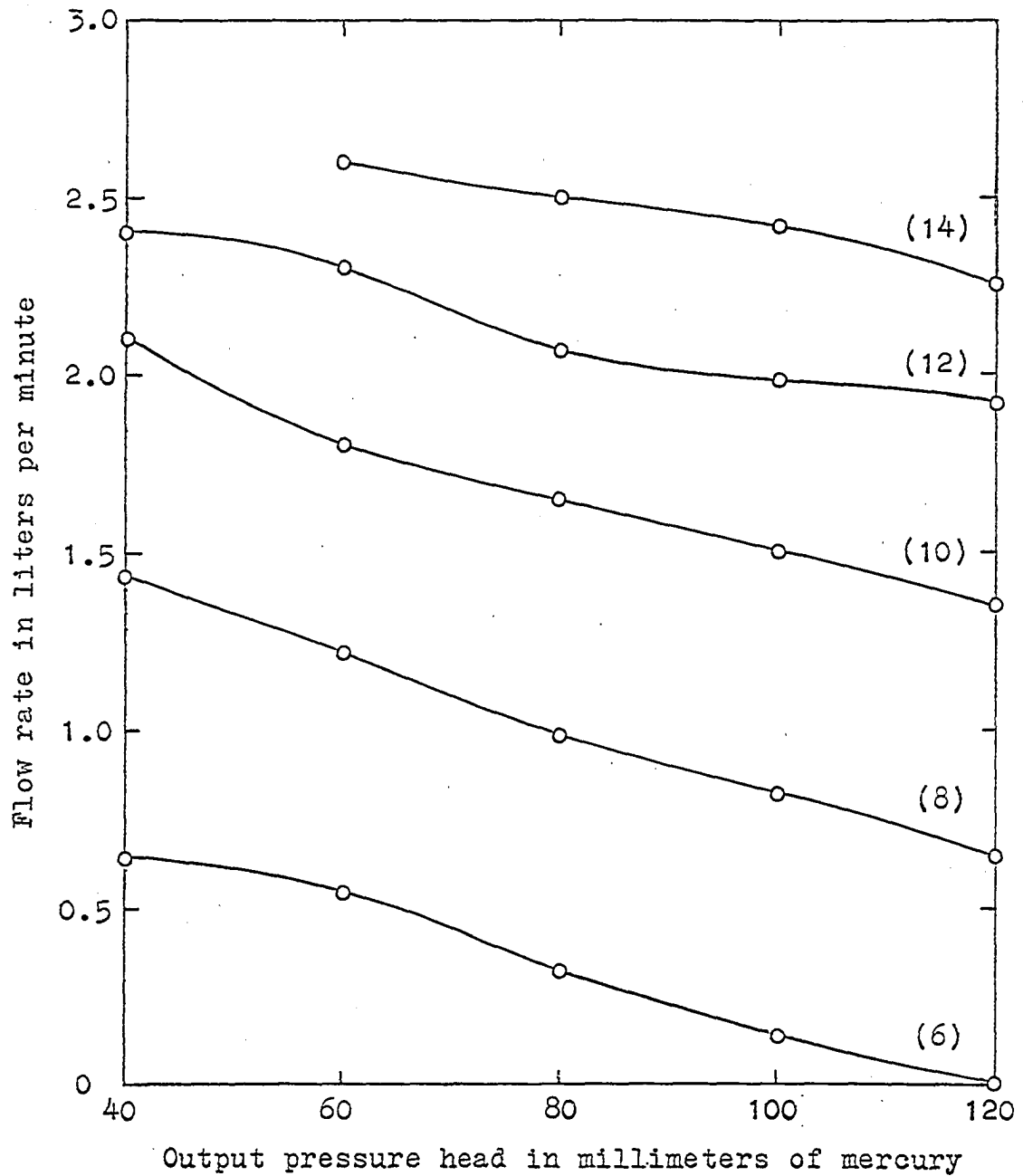


Figure 18. Liquid output of the Model II ventricle as a function of both output pressure head and pulsed air pressure. The number in ( ) is the resting level of the pulsed air pressure in pounds per square inch. The input filling pressure was five mm. Hg.

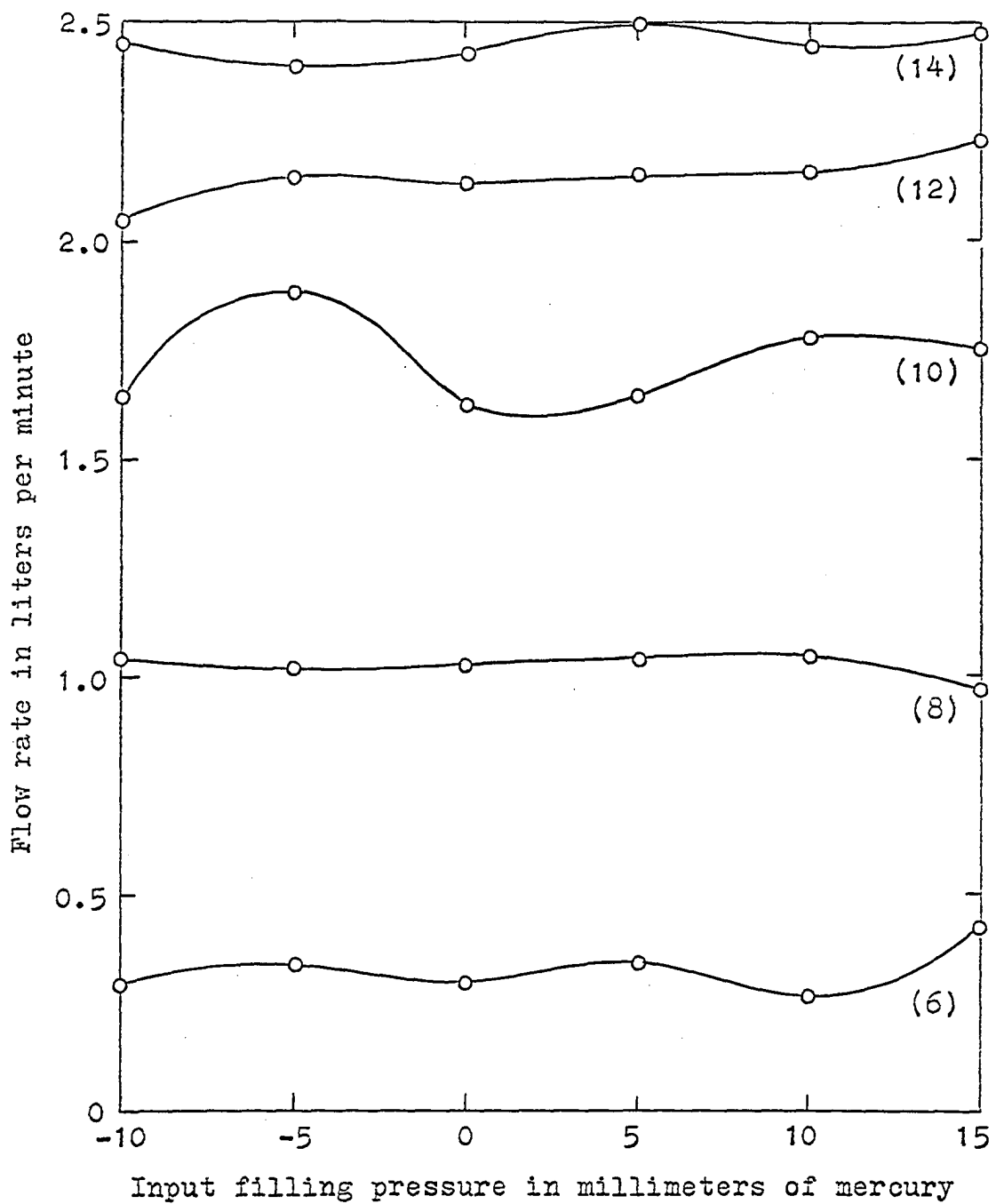


Figure 19. Liquid output of the Model II ventricle as a function of both input filling pressure and pulsed air pressure. The number in ( ) is the resting level of the pulsed air pressure in pounds per square inch. The output pressure head was 80 mm. Hg.

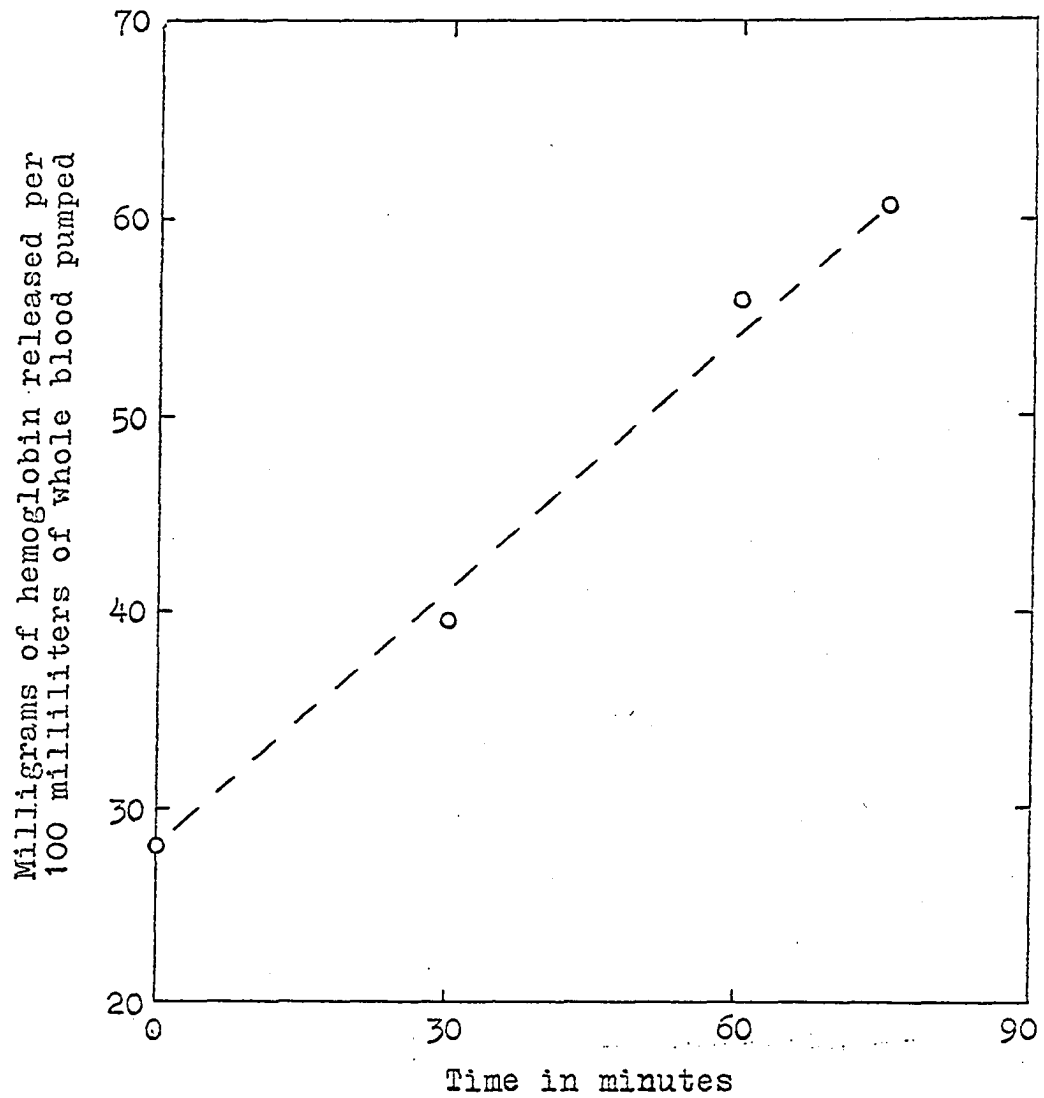


Figure 20. Appearance of plasma hemoglobin as a function of time for a Model II artificial ventricle

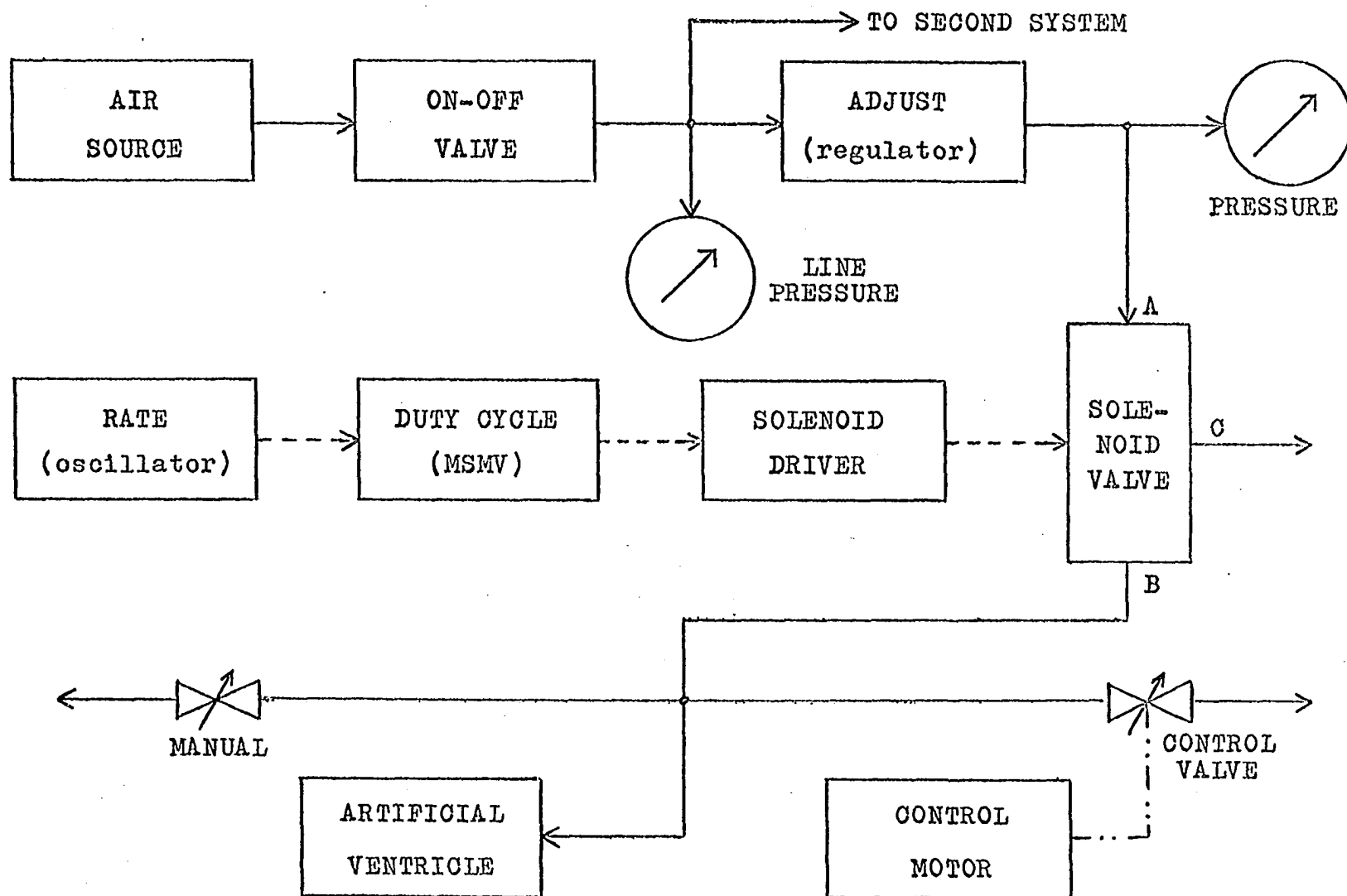


Figure 21. Block diagram of a one-ventricle pneumatic power system



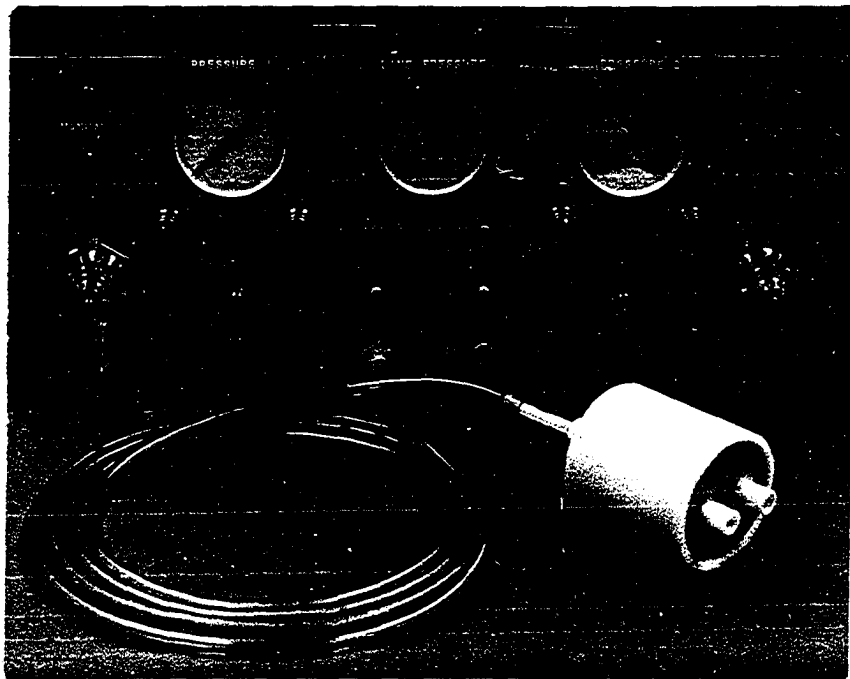


Figure 22. Pressure control module -- front view

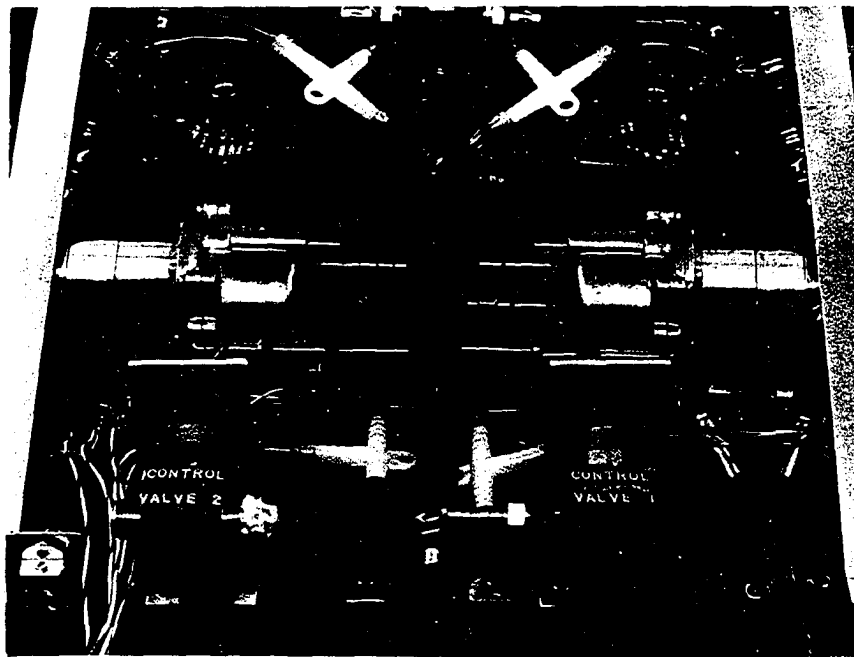


Figure 23. Pressure control module -- rear view

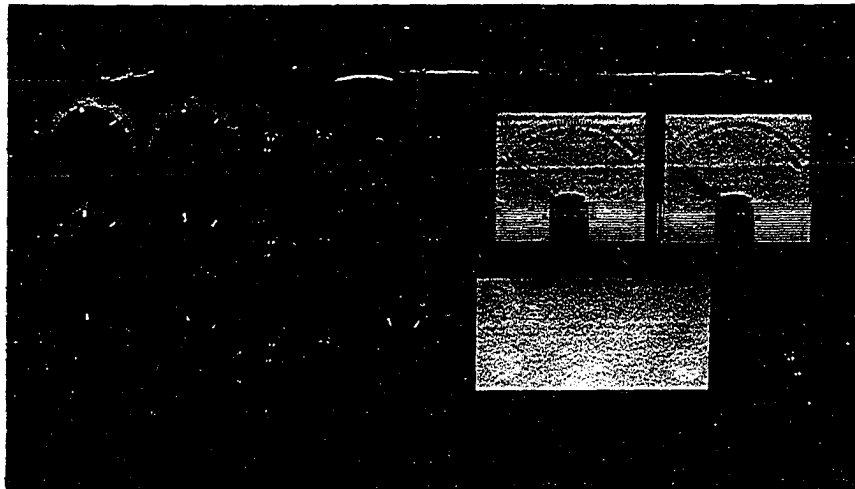


Figure 24. Heart rate and duty cycle module

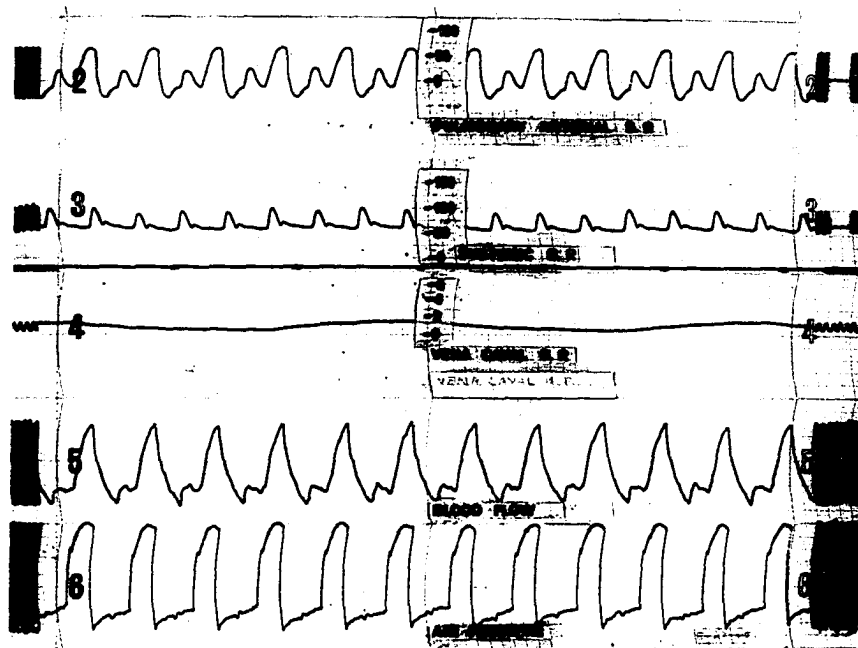
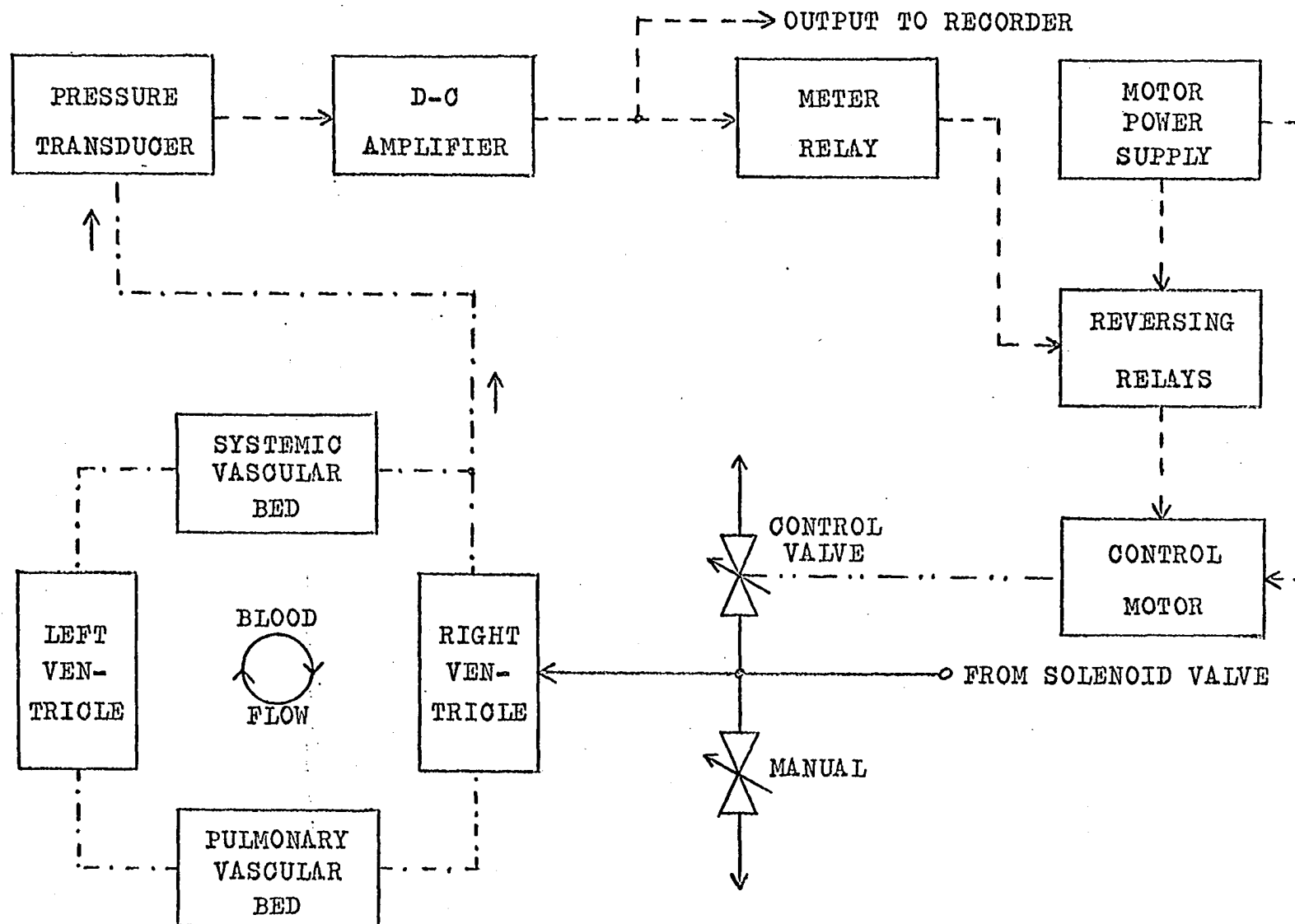


Figure 25. Flow and pressure recordings

Figure 26. Block diagram of a one-ventricle control system and the circulatory system



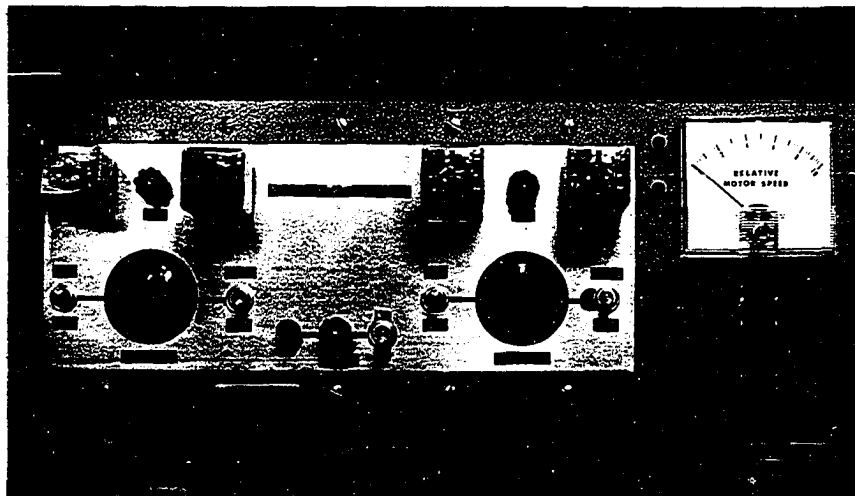


Figure 27. Control motor power supply module

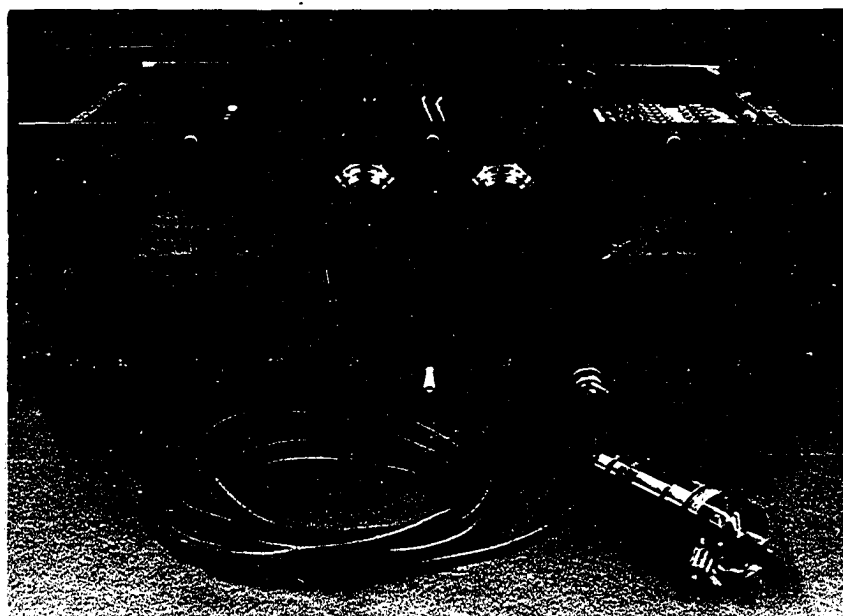


Figure 28. Meter relay module and Statham PR23-1D-300 pressure transducer

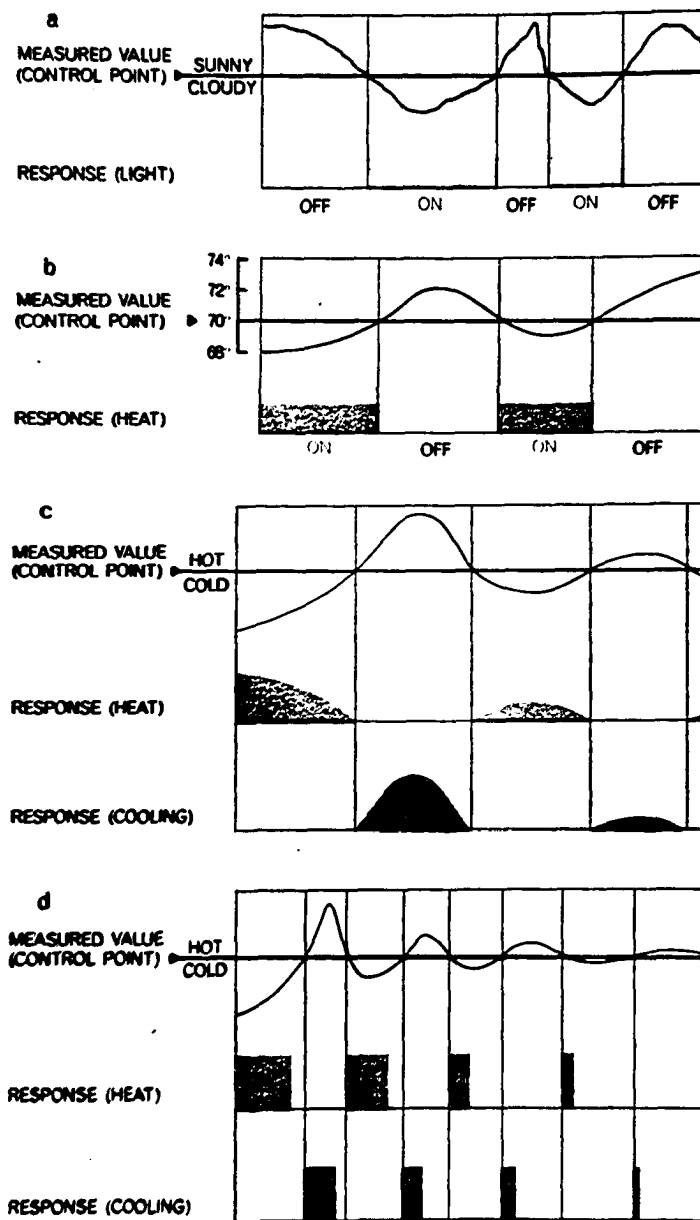


Figure 29. Responses of four control systems  
(Bellman, 11, p. 190)



Figure 31. Schematic diagram of the total  
cardiopulmonary bypass procedure

Figure 32. Schematic diagram of the right  
ventricular bypass procedure



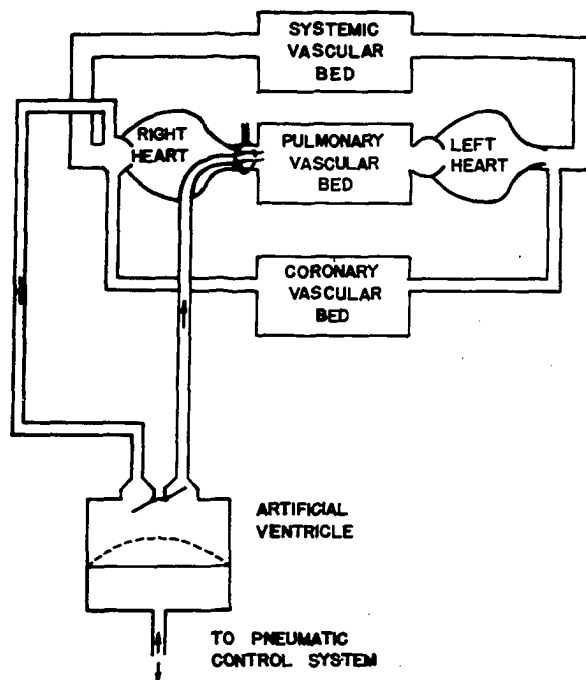
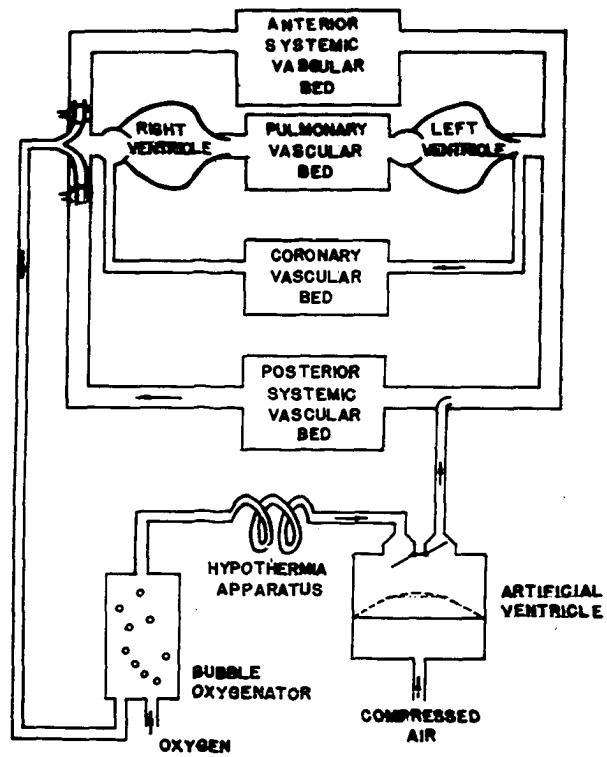
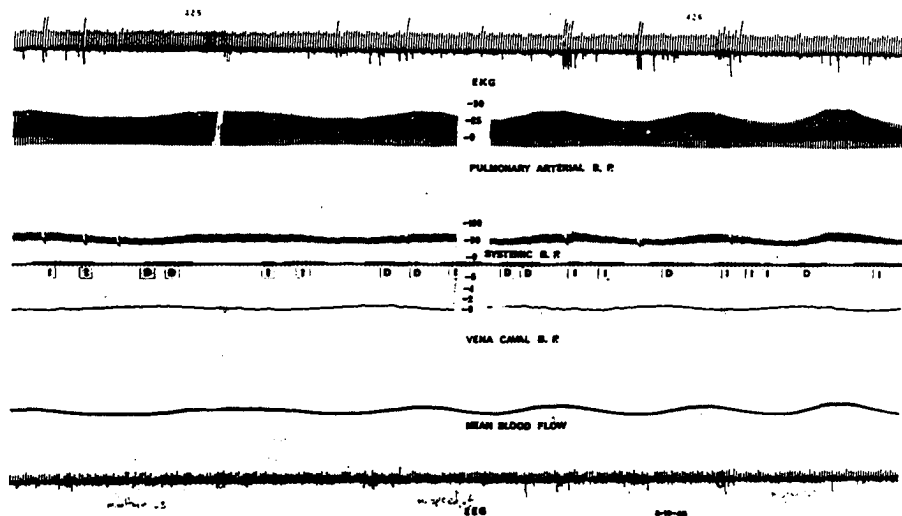
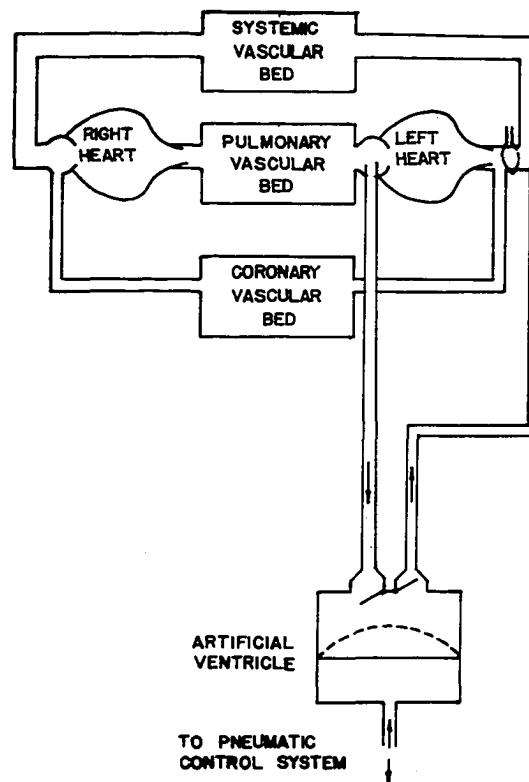


Figure 33. Schematic diagram of the left ventricular bypass procedure

Figure 34. Recordings taken during an in vivo automatic control sequence -- stable oscillating response



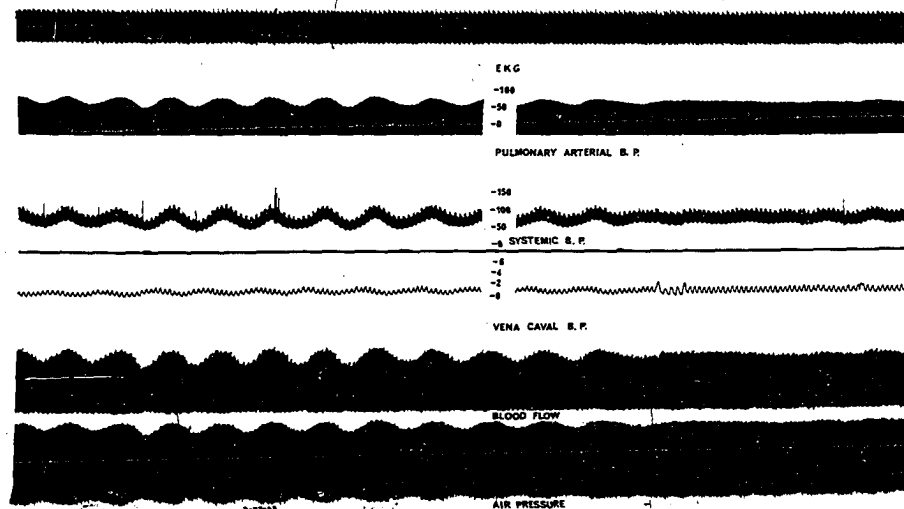


Figure 35. Recordings taken during an in vivo automatic control sequence -- effect of control motor speed on machine response

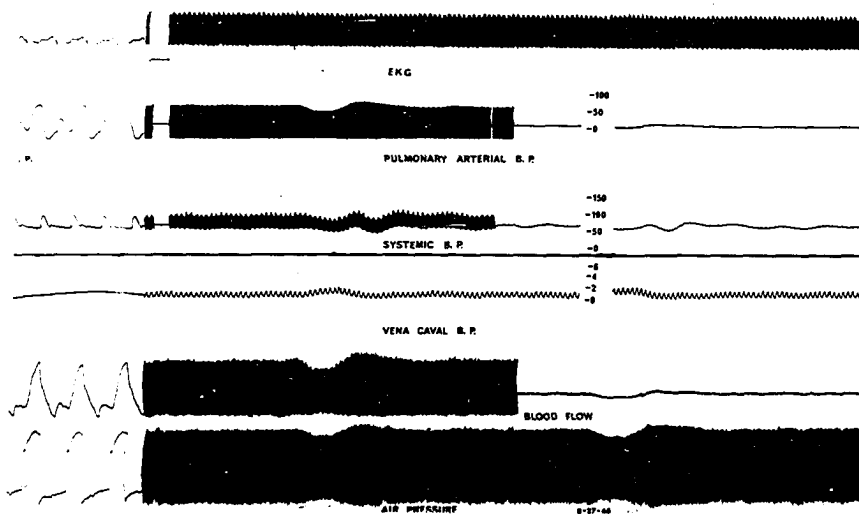


Figure 36. Recordings taken during an in vivo automatic control sequence -- response of control system to an air pressure perturbation

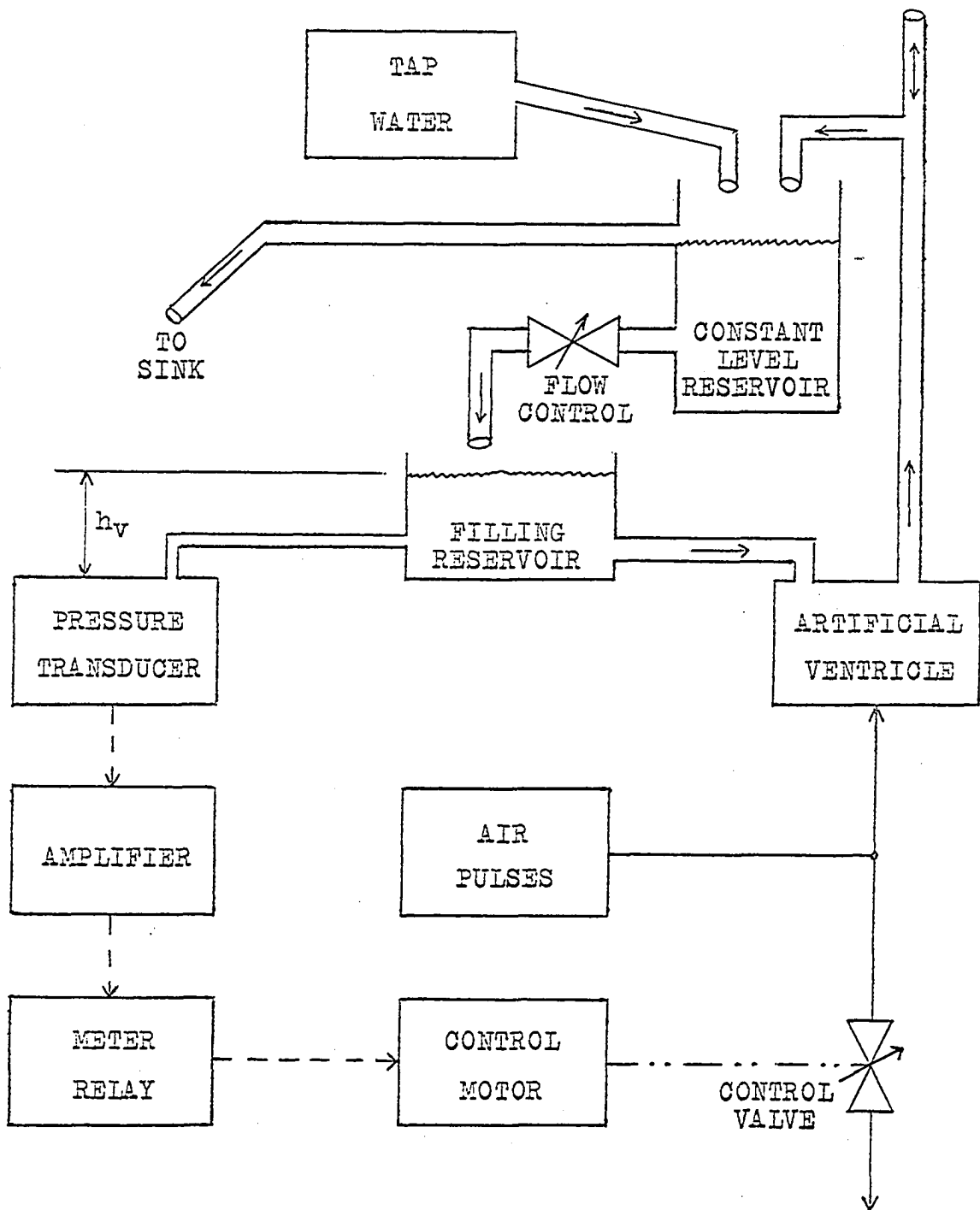


Figure 37. Diagram of the test circulation and its connections to the artificial ventricle system

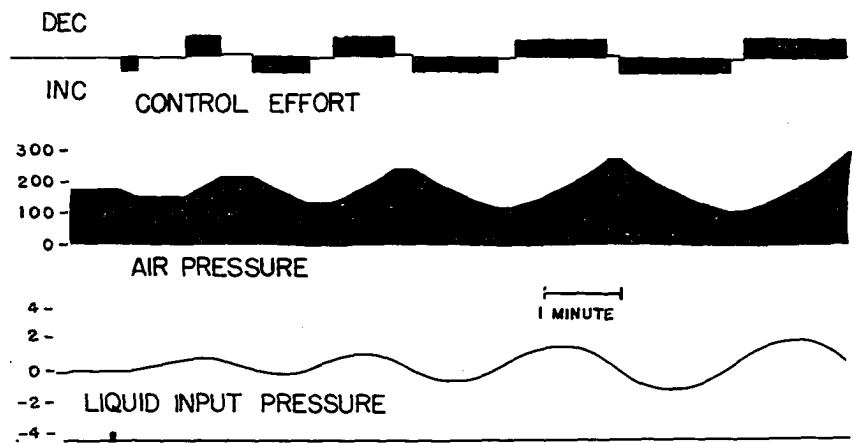


Figure 38. Recordings taken during an in vitro automatic control sequence -- unstable oscillating response

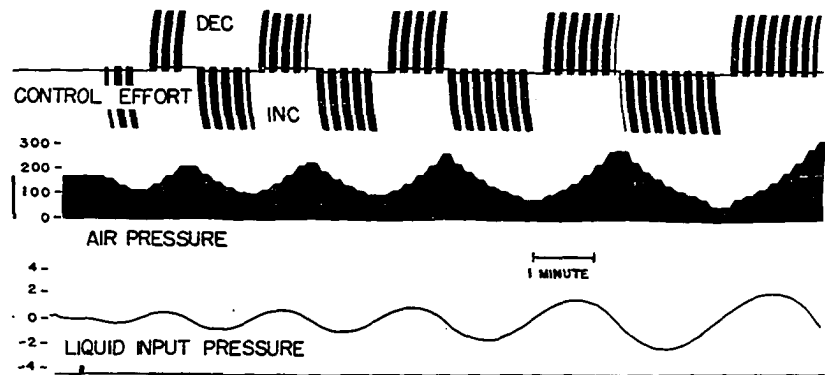


Figure 39. Recordings taken during an in vitro automatic control sequence -- unstable oscillating response with intermittent control motor operation

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TABLE

Table 1. Specifications of the three artificial ventricles

Model	Size in centimeters, length x diameter	Weight in grams	Air chamber volume in milliliters	Diastolic volume in milliliters	Stroke volume in milliliters
I	30.1 x 9.5	406	44 - 196	70	0 - 25
II	7.0 x 6.5	234	15 - 40	34 - 90	0 - 40
III	15.0 x 11.4	666	70 - 200	155	0 - 100